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THE AMERICAN
JOURNAL OF PHARMACY

VOL. 95. FEBRUARY, 1923. NO. 2.

EDITORIAL

THE MISUNDERSTOOD CHLORINE ANTISEPTICS.

When Dakin and Carrel consummated the great discovery that gave surgery and the world the now famous "Dakin Solution," they little knew that their invention was to inaugurate a germicidal fad that has since poured a profusion of chlorine containing compounds into an already bulging materia medica. Not even the most pretentious index of surgical antiseptics can hope to keep pace with the unending trail of organic and inorganic chlorine agents that followed in the wake of Dakin's standardized liquid. Some were good and in their respective fields of usefulness merited at least a transient consideration.

But that is not our concern. We are more genuinely interested in keeping clear in our minds certain undistorted facts so that out of the maze of substitutes, succedanea and alternates we can recognize the original when we have need to recognize it.

Surgeons and pathologists still insist that the aqueous Dakin solution, compounded and standardized exactly as Dakin suggests, is the antiseptic and tissue-cleansing agent *par excellence*. They say that nothing has come since Dakin's discovery to compare in any way with this solution of hypochlorite of sodium. So they persist in prescribing and in using it. Of course, there are practical (but not over-scientific) surgeons who find it less painstaking to opinionate adversely as to the value of the solution. They discredit it without knowing it and without experiencing the good that comes from scientifically using it. And so they do not use it.

That is also not for our comment. But there is another ground upon which we want to lay especial stress. And it is this. Insofar as many surgeons acclaim the value of Dakin solution and want to use it in their practice, it is the business of the pharmacist to see to

it that the surgeon gets precisely what he desires. There must be no misinterpretation of his request, nor a misunderstanding of it.

A large surgical institute in Pennsylvania boasts of the service of many well-known surgeons. Some of these men knew and valued Dakin's solution. They ordered it for irrigating, for bathing tissue surfaces, for douching and for many other purposes. But they failed to get results, and noticed that it did not perform as was its wont in other days. They then instigated an inquiry, and found to their amazement that the pharmacist had accepted the suggestion of a detail man to use, instead of the conventional technic of preparation, a method whereby the mere dissolving of a proportion of an organic compound of chlorine in water afforded an "equally valuable solution."

The pharmacist has no business to accept and put to work such empiric suggestions. There is no excuse for such a deviation of responsibility. Dakin solution cannot be duplicated, in any manner except appearance, by dissolving a little chloramine T or similar compound in water. *It was never made in that way. It must never be made in that way.*

It is a gross injustice to the surgeon and an unwarranted hardship to the patient for the pharmacist or chemist to knowingly or unknowingly perpetrate such a departure from the correct procedure.

We do not think it necessary to return at this time to a careful chemical differentiation of the more important of these chlorine compounds. However, in view of the fact that there is some misunderstanding as to what Dakin's solution really is, it is hardly anachronistic to repeat in brief its correct definition.

"Dakin's Solution (or Carrel-Dakin aqueous solution) is a freshly prepared aqueous solution of sodium hypochlorite, practically devoid of free alkali, and containing from 0.45 to 0.5 per cent. of sodium hypochlorite." It is prepared by the interaction of chlorinated lime, sodium carbonate, and sodium bicarbonate in distilled water, or by the dilution of an alkali-free concentrated solution of sodium hypochlorite. It is always standardized before dispensing. It must not be prepared in any other way.

I. G.

THE PHARMACIST AND THE HOSPITAL.

The pharmacist often occupies an anomalous position in the hospital organization. The pharmacy department represents a very valuable element among the working units of the institution, but with the theorists who control the policies and destinies of the hospital the work of the department is often greatly underrated. The substantial reason for this belittlement of its value lies probably in the fact that the management confuses the issues and sees for this department only a small share in the hospital's quota of "service rendered." So we find, despite the advancement of hospital organization, despite the settlement of an accepted standard for most hospital departments, the pharmacy is still unstandardized.

There are some who like it so. But the truth still stays and points to a conviction that if we want to keep abreast of modern processes of organization we also need to leave with finality the old hit-or-miss methods which are still practiced in many a hospital pharmacy.

We particularly point to one factor of non-standardization, which permits a hospital pharmacy to function without the supervision of even a part-time pharmacist. Witness the advertising columns of a recent issue of a medical journal and see in the "Wanted" column paragraphs such as these: "Wanted: Nurse with experience in dispensing drugs." "Laboratory technician who knows how to handle drugs." We, of course, read between the lines when we draw the inference that such services do not come under the supervision of a pharmacist in charge. Experience and our information, however, teach us that in many small hospitals this manner of conducting the pharmacy with a nurse or a technician frequently obtains. Granting that such persons have some smattering of dispensing knowledge, we can, however, very safely and emphatically state that to turn such people loose in a pharmacy constitutes a menace to the welfare of the hospital's tenants that is nothing short of criminal.

Annals of hospital practice frequently hide a dismal chapter that tells the story of a disastrous error occurring in the nurse-conducted pharmacy. Only recently we read of oxalic acid being dispensed in place of magnesium sulphate by a probation nurse "in charge" of a hospital dispensary. These things may happen in any

pharmacy, but certainly the chances are not so great when a well-trained person is in charge of that important department.

The management that aims to conserve a little money by functioning without a pharmacist is penny wise and pound foolish and is not looking to the welfare of the patients. It is false economy, indeed, that permits a person ignorant of the value and virtue of drugs to be responsible for their purchase, their storage and preparation.

A recent investigation of a small hospital pharmacy in charge of a graduate nurse, untrained in pharmacy, brought to light the following interesting facts: On the stock shelves were two pound packages of hydrocyanic acid of an ancient vintage, brown with cyanogen but vainly ready to do its bit to cure a cough when called for. Fluidextract of ergot was apparently purchased in gallon lots and used at the rate of a pint a year. All of the tinctures were purchased in bulk and the hospital paid real money for this material, utterly disregarding the monetary benefits that accrue from making tinctures with tax-free alcohol. Lime water was actually prepared from chalk masquerading under the name of lime.

But the most insidious danger of all in these loosely conducted pharmacies is in the dispensing of unreliable and worn-out drugs. For after all even the most nihilistic surgeon and internist depend a good deal on drugs. The suprarenal extract that saves the day when surgical shock frays the bare thread that keeps life suspended; the cocaine solution that takes burdens of pain from the shoulders of the long suffering son of man; the chlorine antiseptic that keeps clean the surgeon's field of battle so that healing nature may unhindered work its blessed ways—all of these things must be prepared by trained hands backed by a careful mind, and not dispensed at random by persons unaware of their nature and ill-trained to compound and combine them. The greatest handiwork of the able surgeon may fall by the wayside unless the therapeutic agents which he orders in the wake of the operation are safely and accurately prepared. And this is, indeed, the most convincing argument of any in favor of placing none but a trained pharmacist in charge of the hospital pharmacy.

For there comes coincident with this establishment of a responsible trusteeship over the pharmacy a sense of security and protection not otherwise afforded.

I. G.

ORIGINAL ARTICLES

THE DETERIORATION OF DRUGS AND HOW TO PREVENT IT.

By Joseph W. England, Ph. M.

When the public buys drugs of a drug store, it buys something more than drugs—it buys "service," which service includes the surety that the goods bought are of standard purity, quality and strength.

It is not enough that the pharmacist buys drugs of guaranteed standard. The public expects him to examine his goods when he buys them from time to time, to determine possible deterioration, and to destroy deteriorated goods. It buys his technical knowledge and skill as well as his drugs.

The wholesale druggist and manufacturer guarantee their goods as they sell them, but they cannot be expected to continue their guarantee after the containers have been opened and the goods have been unduly exposed to sunlight, extreme heat, cold or moisture, or have been kept under such conditions as would, owing to the nature of the goods, cause deterioration.

Whatever differences of opinion may exist as to the best conduct of the modern drug store, to meet the needs of the public, the fact remains that the drug store is, or should be, primarily and fundamentally, a store for the sale of "drugs," and when it ceases to be this, it ceases to be a drug store, by whatever name it may be called. It is simply a merchandizing emporium. True, such a store may sell "package drugs," but what guarantee has the public that the same critical examination of such goods is made as by the man who has a professional reputation at stake?

Such being the case, the conduct of a "drug store" carries with it certain duties and responsibilities, not the least important of which is the critical examination of the stock, as occasion may require. The biggest asset of a drug store is the personality of its proprietor and this either inspires respect or the reverse according to the manner in which the proprietor conducts his store and treats his patrons.

To keep drugs from deterioration is to ensure quality and to save money and reputation. As the late William B. Thompson once said: "Business logic: Poor drugs—poor result. Poor result—poor reputation. Poor reputation—poor business."

The drug business is one of multitudinous details. The average drug store stock represents hundreds if not thousands of articles. Our company (Smith, Kline & French Co.), for example, carries over 100,000 items, including similar articles of differing strengths.

The physical conditions under which drugs are kept is of great importance. Drugs vary in characteristics. Some are organized, some inorganic and some organic. Many are prone to change on exposure to air. Some absorb gases, odors and moisture, and some give off water or gases. Some undergo oxidation, some reduction and some hydrolysis. Some undergo structural change and some chemical change. The changes depend upon the nature of the drug, its physical character and the conditions under which it is kept.

The kinds of containers are various, being made of glass, tin, wood, cardboard, paper, etc., and their protective value is usually in the order named, as is also their cost. In the marketing of goods, the cheapest container is used, all other things being equal, *but in many cases there is no substitute for glass.*

It will be impossible, at this time, to detail the proper container for each and every drug, but the writer will endeavor to lay down certain general principles, as illustrated by certain drugs, as follows:

Vegetable drugs, whole or powdered, should be kept in tight containers in a dry place; some drugs like cantharides, rhubarb, aconite, etc., are attacked by insects, and these can be protected by adding a little chloroform or carbon tetrachloride, from time to time, which can readily be removed by heat when the drug is to be used.

Drugs kept in drawers contiguous to the drawers of odorous drugs are very apt to absorb and become tainted with foreign odors.

Volatile oils are best kept in original containers in a cool place protected from light. The terpene-containing oils are very prone to become terbinthinate. Orange oil and lemon oil are best kept by diluting them with an equal volume of alcohol (when they are to be used for making elixirs), and employing double the quantity of the oil specified in the formulas.

Fixed oils are apt to become rancid, especially in the presence of moisture, and should be kept in a cool, dark place. With all oils it is good practice to carefully wipe the lips of the oil bottles after pouring out the oil.

Lard exposed to the air absorbs oxygen and gradually becomes

rancid. It must be kept in a cool place in a well-closed container which is impervious to fat; benzoinated lard is much less prone to change, but it will change in time if not properly kept. Wool fat and hydrous wool fat should be kept in the same way as lard; also, cerates and ointments. Old porcelain ointment jars with crazed surfaces are especially apt to induce rancidity in fats, cerates, etc.

The heating of ointments to high temperatures may cause melting and separation of active ingredients; long-continued exposure to air, warmth and moisture may cause granulation and rancidity. Ointment of belladonna should be made extemporaneously, or kept in small quantities only, as the alcohol it contains volatilizes and the residual ointment, with its about 10 per cent. of water, is apt to granulate or to mould. Zinc ointment granulates readily, and citrine ointment darkens readily. Keep ointments in amber jars, tightly closed, in a cool, dry place, protected from light.

Pepsin and pancreatin are hygroscopic and their preparations lose in strength on keeping.

Biologic drugs, such as vaccine virus, antidiphtheric serum, antitetanic serum, etc., gradually lose in potency, even if kept under the best of conditions, the loss being more rapid at high temperatures than at low. They should be preserved at a temperature between 4.5° and 15° C., and protected against light. The best storage place is an ice box or refrigerator reasonably well supplied with ice. It is vitally important that this stock be kept fresh at all times. Small quantities only should be bought at a time, or enough to meet current demands. If the time-limit for exchange for any of the products has expired, return at once to the manufacturer for credit or replacement.

Many chemicals are susceptible to change; those which do not change are usually marketed in tin, wood, carton or paper (plain or paraffined); and those which do change, in glass.

Chromic acid or trioxide is a powerful oxidizing agent and in contact with organic substances is liable to explode violently; similar oxidation will result with nitric acid, potassium chlorate, potassium permanganate or sodium peroxide. Hence, such compounds should be kept in glass containers. Silver nitrate "becomes gray or grayish black on exposure to light in the presence of organic matter" (U. S. P. IX, 61), and hence should be preserved in dark amber-colored vials protected from light. Pyrogallic acid is a powerful reducing agent,

absorbing oxygen greedily, and should be kept in tin or glass. Some years ago, before its properties were so well known, the writer bought five pounds of a chemical manufacturer and it was delivered in paper, and stored temporarily in a wooden drawer. A month later, when the drawer was opened the paper of the package was black—it had been slowly burnt or carbonized.

Camphor, menthol, thymol and hydrated chloral are slowly volatilized and should be kept in well-stoppered containers.

Ether is exceedingly volatile, and its vapor highly inflammable. It must be kept in well-stoppered containers remote from fire and protected against daylight, or it will decompose. When ether is to be used for anesthesia, it must "be dispensed only in small, well-closed containers" and must "not be used for this purpose if the container has been opened longer than twenty-four hours" (U. S. P. IX, 32). It should be administered by daylight or electric light.

Even greater care must be used with chloroform. It must be kept in well-stoppered bottles in a cool place protected from light. It should not be kept in tin. Recently large quantities of Government chloroform marketed in tin decomposed and had to be withdrawn from sale. It is rapidly decomposed when its vapor comes in contact with exposed gas light, evolving chlorine gases, which are exceedingly irritating and even dangerous to the patient. It should never be administered by gas light, unless the flame be protected by a glass case and ample provision made for the rapid escape of decomposition products from the room.

Some chemicals are affected by heat, light and air. Thus, benzoic acid is volatile and darkens with light. Citric acid effloresces in warm air. Glycerin, lactic acid and sulphuric acid absorb moisture and become weaker in strength. Oleic acid darkens in color and absorbs oxygen. Salicylic acid and salicylates become pink on contact with iron and moisture, and a damp steel spatula should never be brought in contact with them. Tannic acid turns dark on exposure to air and light. Hence, the necessity of keeping all such substances, as these in well-closed containers in a cool place protected from light. Sugar of milk absorbs any and all kinds of odors, even the odor of wood if kept in barrels of odorous wood, and must be kept well-protected. Deliquescent salts like the potassium salts, and efflorescent salts like the sodium salts, are best kept in glass containers, although salts of the type of sodium phosphate, are often sold in paraffin-lined cartons or wrapped in waxed paper and paper, for economy.

Epsom salt and Glauber salt are efflorescent also. The scaled salts of iron, generally, are deliquescent and affected by light. They should be kept in amber-colored, well-stoppered bottles.

Certain ammonia salts are more or less unstable—benzoate, carbonate, iodide and valerate. The official carbonate consists of acid carbonate and carbamate, and its "masses" are best preserved by wetting them occasionally with a small quantity of stronger ammonia water, whereby they remain hard and translucent.

Alkaloids and alkaloidal salts keep reasonably well if preserved in well-closed containers; small quantities are best marketed in glass. Physostigmine (or eserine) salicylate acquires a red tint when long exposed to light and air, and its solution—used for eye treatment—kept in bottles becomes colored from the alkalinity of the glass of the bottle: it is best dispensed dissolved in a solution of boric acid.

Much loss results from the improper storage of the certain chemicals and products containing volatile compounds, *e. g.*, amyl nitrite (which should be kept in tight glass-stoppered vials), ether, chloroform, ammonia water, alcohol and medicated spirits, generally. Few realize the loss by evaporation that results when such products are kept in stock containers only partially filled; every time the container is opened there is a loss of active ingredient.

A striking example of such loss is spirit of nitrous ether. Experiments by John G. Roberts, of our Analytical Laboratory, have shown that "ethyl nitrite is easily dissipated from its alcoholic solution; that the action of sunlight is very destructive to it in flint glass containers; that partly filled containers are objectionable, and that it is bad practice to dispense numerous orders from the same container. The ideal method of storage is small *completely filled* amber bottles kept in a refrigerator or ice box."* It should be kept, of course, remote from fire. The best procedure for the retail druggist is to buy tubes of concentrated nitrous ether, make his own spirit, bottle in amber bottles completely filled, and keep them cold. This is worth while, because spirit of nitrous ether is one of the products often

*A one-quart stock bottle was filled with spirit of nitrous ether, and two ounces removed every day for 15 days, for assay. The decrease in ethyl-nitrite was from 5.22 per cent. to 4.04 per cent., or over 22 per cent. Four ounces of the spirit was placed in a pint stock bottle, placed on shelf, and its strength after 21 days was reduced from 4.58 per cent. to 2.71 per cent. or over 40 per cent. (John G. Roberts.)

collected by inspectors of State boards of health or pharmacy for examination as to strength or departure from official standard. And yet I have repeatedly seen, in retail drug stores, shelf bottles of spirit of nitrous ether only partially filled and of a deep yellow color, showing decomposition. Loss of active ingredients also take place in partially filled bottles of spirit of ether and spirit of chloroform, though less rapidly than with spirit of nitrous ether; with spirit of camphor the preparation becomes stronger through loss of alcohol contents.

Aromatic waters are saturated solution of volatile oils in water. If kept too cold, they become cloudy, or if kept too long they lose flavor and strength; and with rose water and orange flavor water a mouldy growth firms.

Solution of ammonium acetate should be faintly acid from acetic acid (and not only from carbonic acid), and should be made and dispensed as needed.

Solution of calcium hydroxide (lime water) absorbs carbon dioxide from the air and precipitates calcium carbonate. It should be kept "in well-filled, tightly stoppered bottles," as officially directed, and the saturated solution only dispensed. Solution of lead subacetate (lead water) undergoes similar change and must be similarly preserved.

Solution of hydrogen dioxide is exceedingly prone to change. In fact, its readiness to change—to give up oxygen in contact with organic matter—is its feature of greatest value. It should be "preserved in a cool place protected from light, and upon removing the stopper from the bottle, not more than a slight pressure should be observed" (U. S. P. IX, 246). The stopper of the bottle should be coated with paraffin or some non-oxidizable coating or replaced by a plug of purified cotton.

Solution of potassium hydroxide and solution of sodium hydroxide must be kept "in bottles of hard glass with rubber stoppers or glass stoppers coated with petrolatum" (U. S. P. IX, 252, 255). Cork stoppers should never be used as the caustic alkali destroys the corky tissue and darkens the solution. These solutions sometimes become turbid by the precipitation of silica, which can be removed by filtration through asbestos fibre in a glass or rubber funnel.

Solution of iron and ammonium acetate is not difficult to keep if the solution of ammonium acetate used be slightly acid (from

acetic acid). It should be made extemporaneously as needed for dispensing. The most convenient method is to use the so-called "Basham's Elixir," now commercially obtainable.

Solution of magnesium citrate should be made of "boiling water and kept in the bottle on its side in a cool place, preferably in a refrigerator," as officially directed. Not more than a few days' supply should be kept on hand. Complaint is sometimes made that this solution is too sour to be pleasing, especially to children, in which cases the best plan is to advise the addition of a small quantity of sodium bicarbonate (or enough to cover a quarter), to the bottle-full, which will reduce the acidity and make the solution much more acceptable.

Solution of potassium citrate should always be freshly made as needed and be faintly acid from free citric acid.

Physiological solution of sodium chloride, or normal salt solution, is used for washing mucous surfaces—nose, throat, etc., and for injection into subcutaneous tissue. For the former purpose, the usual practice is simply to dissolve a normal salt tablet in a four-ounce bottle of boiling water and use. For injection, the procedure of the Pharmacopœia should always be followed, *i. e.*, sterilization of the solution by heating in an autoclave, under steam pressure at a temperature of from 115° to 120° C. for fifteen minutes, or by boiling at least one hour, preserving it in a sterile condition. This solution should not be used after it has been made forty-eight hours (U. S. P. IX, 255).

Liniments containing alcohol should be protected against the loss of alcohol, and chloroform liniment, especially, against the loss of chloroform. Chloroform liniment is often the subject of board of health or board of pharmacy investigations.

Chalk mixture should always be made extemporaneously.

Mucilage of acacia, which is officially made from gum acacia, is apt to decompose during the summer, and should then be made extemporaneously from granulated acacia; the latter product is not as clear as the official, but is just as good therapeutically.

Of the official spirits, compound spirit of orange will keep reasonably well "in completely filled, well-stoppered bottles, in a cool and dark place," as officially directed. Spirit of nitrous ether has been previously discussed. Spirit of glyceryl trinitrate (spirit of nitroglycerin), the Pharmacopœia states, must be preserved "in well-stop-

pered bottles in a cool, dark place, remote from fire. Great care must be exercised in dispensing, handling, package, transporting and storing this spirit, since a dangerous explosion may result if any considerable quantity of it is spilled, and the alcohol wholly or partly lost by evaporation. If, through accident, it is spilled, a solution of potassium hydroxide must be poured over it at once to effect partial decomposition" (U. S. P. IX, 407). Spirit of peppermint and spirit of spearmint must be preserved in amber-colored bottles, as officially directed, in order that their chlorophyl may not be bleached by light.

Fluidextracts after being made should be aged for at least one month and kept in amber-colored bottles protected from extremes of temperature. Even with this precaution some fluidextracts precipitate on keeping, especially those made in warm weather and kept until winter, carrying down active as well as inactive material; in which case, measure the volume of the liquid, filter, and make up the volume with proper menstruum. If the fluidextract was originally standardized, the clarified product must be standardized, also. Physiologically tested fluidextracts—aconite, cannabis, convallaria, digitalis, ergot and squill should be purchased in small quantities only to meet current needs, as they tend to deteriorate if kept for long periods.

Extracts when freshly made are of "pilular consistence," but often dry out and become hard when kept in a warm place in a loosely covered container. They must be kept in tightly covered amber-colored glass, glazed earthenware containers or porcelain jars, protected from air and in a cool place.

Powdered extracts are more or less hygroscopic and harden on exposure to air, especially in loosely stoppered bottles. They must be kept in tightly stoppered, wide-mouthed, amber-colored bottles, and in a cool and dry place.

Tinctures are less liable to change than fluidextracts, but they do precipitate at times, and should be kept in tightly stoppered, amber-colored bottles in a cool place, protected from extremes of temperature. If precipitation occurs, measure the liquid, filter and make up the volume with the proper menstruum. If the tincture was originally standardized, the clarified product must be standardized also. Tinctures become stronger on standing in partially filled stock containers by reason of loss of alcohol. Tincture of iodine is a no-

table example of this. Physiologically tested tinctures—aconite, cannabis, digitalis, strophanthus, etc., should be bought only in small quantities to meet current needs, as they tend to deteriorate if kept for long periods.

Elixirs are delicate in their reaction to physical influences and exceeding care should be used in making and storing them. Elixirs containing iron are liable to darken by exposure to light. The flavoring substances, usually volatile oils, should be absolutely fresh and of the finest quality. They are best preserved in tightly stoppered bottles at ordinary room temperature protected from light.

Effervescent citrated caffeine, effervescent potassium citrate, effervescent sodium phosphate, and other effervescent salts slowly decompose on exposure to air containing moisture, losing carbonic acid gas, and should be kept in suitable containers and sealed tightly. Decomposed effervescent salts are literally "stale, flat and unprofitable."

Emulsions kept under ordinary conditions often "break" and on exposure to air become rancid. They should be kept in well-stoppered glass containers, and not be subjected to extremes of temperature. They should be made extemporaneously, as far as possible.

Syrups that contain too little sugar ferment; syrups containing free acid, such as syrup of citric acid, syrup of hydriodic acid, syrup of orange, syrup of calcium lactophosphate and syrup of squill, have their sugar inverted in time, and become "musty." Syrups of the hypophosphites, especially the compound syrups containing iron, are liable to change. Syrup of ferrous iodide discolors and should be "preserved in completely filled, tightly stoppered bottles," as officially directed, but the best plan, in the writer's experience, is to make the syrup in small quantities to meet current needs from the concentrated solution of ferrous iodide and syrup. Reasonably small quantities only of syrups should be kept in stock.

Compressed tablets in large quantities are usually sold in tin or wood containers, and in small quantities in glass, as are tablet triturates and hypodermic tablets. Glass is the best container, because tablets contain moisture and sometimes volatile ingredients, and on exposure to air lose both and become harder and more difficult of disintegration. Especial care should be used in the storage of the so-called "dispensing" tablets, so that they shall not be mistaken for the usual tablets. Tablets of corrosive mercuric chloride should be dispensed in securely stoppered glass containers with a red "poison"

label and the content of corrosive mercuric chloride stated on the label.

In conclusion, may I say that no matter how skilled the service of a pharmacist may be in the care of drugs, this avails little to the "ultimate consumer" if such care be not accompanied by equal care in compounding and dispensing; and I would like to suggest to pharmacists generally the following: "Use the best balances and scales you can buy, and keep them clean and in good working order, examining them periodically for accuracy. Use weights and graduated measures only that are guaranteed and keep them clean with soap, brush and water, testing them frequently. Buy official drugs of official standards only and unofficial drugs of dealers who will guarantee them. Use the latest editions of the Pharmacopeia and National Formulary and observe strictly their procedure and standards. Use the apparatus directed by these authorities and needed for accurate prescription work."

Such a procedure is absolutely essential for accurate work, and its adoption will more than pay, not only in moral satisfaction, but in increased business.

"Quality drugs" and "quality service" are entitled to fair and reasonable compensation. "The laborer *is* worthy of hire," but not to an undue return. If skilled service is given to the public, such service should be adequately and fully paid for, but to overcharge, or to give unskilled service and charge for skilled is both unjust to the public and bad business.

BACTERIAL PREPARATIONS IN COMMON USE.

By Louis Gershenfeld, Ph. M., B. Sc., P. D., Professor of Bacteriology and Hygiene.

(One of a Series of Popular Lectures Given at the Philadelphia College of Pharmacy and Science.)

The layman generally thinks of bacteria as injurious and undesirable invaders. Such opinion and thought have been common, because the average individual is more apt to regard only bacteria that cause disease and diseased conditions. It is not a frequent occurrence for the layman to hear of or come in contact with the useful microorganisms. There are, however, many products which are really bac-

teria and extensively used by everyone but not generally regarded or thought of as being bacteria.

This evening there will be no attempt made to discuss the bacteria that are of value in industries, and in the production of desirable products. Neither will there be considered the many bacteria that produce disease. I will venture to ask your attention to a consideration:

First, of living bacteria sold and used as such in the treatment of diseased conditions.

Second, of dead bacteria or of attenuated bacteria (*i. e.*, bacteria that have been so treated that they have lost their power of producing disease), that are used in the prevention, to assist in the diagnosis, and in the treatment of diseases, which they in their original living condition cause.

Third, of preparations made with bacteria as a starting point, which are subsequently used to prevent, to assist in the diagnosis, and to treat diseased conditions caused by these same bacteria, when in a living and actively growing condition.

May I, at this time, impress upon you the fact that it is not advisable for the layman to attempt to use these preparations without the advice of an attending physician or other competent authority. It is due to the misuse and abuse of preparations of this kind that individuals pass unwarranted judgments concerning them. This holds true even for the simple yeast preparations. Some of the latter have been extensively advertised and exploited with false claims. Even the simple yeast cake is contraindicated in certain conditions and in others should be employed judiciously either with or without other medications, as the practitioner may see fit depending upon the existing findings.

There are many individuals who refuse medication or treatment with some of the preparations which will be discussed. This is due to the prejudiced ideas that belong in days gone by. If I can possibly succeed in changing such thoughts or if by informing you of the methods of preparation, the mode of application or administration and the function of these products, you will co-operate in the future with the medical profession, I will think my time here this evening well spent.

Of the first class I mention the following three micro-organisms which the layman occasionally hears of: Yeast, Bulgarian Bacillus, and Bacillus Acidophilus. These are sold and used in their living condition.

To the scientist, the term Yeast includes a large group of oval or round bacteria about one-four-thousandth of an inch in diameter and which multiply by a process known as budding. Each yeast cell, about twenty minutes after its existence, develops a slight projection or bud. The latter grows until it is nearly as large as the original cell. When ten to fifteen such buds are formed, they separate. These buds, now independent cells, live a separate existence and repeat the process of reproduction, if conditions are still favorable for their growth and development.

In this yeast group there are specific members, some of which are disease producing and others of value in industries. Many of the members are non-disease producing, while some are not desired in the industries, as they interfere with the production of specific end substances.

The layman uses the term yeast as a commercial term. The latter is applied to a specific member (the saccharomyces cerevisiæ), which is manufactured and sold in bulk. Such packages consist of millions and millions of these cells of the specific member (as mentioned) pressed together in a solid mass.

Pasteur was the first to describe and give the characteristics of the yeast group. He observed them while investigating the various phases of fermentation. The study of this group was taken up by other investigators. Today considerable data is available concerning the important part the commercial yeast plays in the production of alcoholic drinks. We are told it is the little things in life that count. You are well aware the trouble that these little yeast cells are causing in the proper enforcement of the Eighteenth Amendment to our Constitution. Home-made alcoholic drinks, palatable, but more frequently non-palatable, are always possible with yeast around.

You are all familiar with the part this same commercial product plays as a leavening agent in bread. Yeast was employed as a curative agent by Hippocrates, and from his days to the present time articles on the therapeutic value of yeast have appeared. The most careful and most thorough studies on the curative value of yeast have been done within the last five years by many well known

investigators and clinicians. It is the opinion of some of these men that yeast, because of its vitamine content, is an efficient food and if controlled properly will be found to assist in the increase of appetite which will in turn mean more utilization of other nourishing foods.

It was also found that yeast, as a food, aids in bringing about a natural uniform elimination of waste. Besides this natural laxative effect, it will in some cases check putrefaction in the intestines. This it does due to the fact that the substances produced when yeast causes fermentation are such as to stop the further growth and development of the organisms that are present causing the putrefaction.

Yeast, acting as a food, aiding digestion, assisting to create an appetite and properly eliminating the waste materials, is therefore of value as an aid in the treatment of some diseases in which an increase of resistance is desired. It is with this thought in mind that yeast is used as an aid in the treatment of boils, carbuncles, acne, and other conditions where pus is produced. The market has been flooded with all kinds of yeast tablets and yeast preparations, but most practitioners have found that it is best and cheaper to use fresh yeast. The form supplied as the yeast cake, with which you are all familiar, is to be preferred. Dried yeast preparations have been found to possess a diminished activity as compared with the fresh cakes. The yeast can be used in conjunction with any other medicinal agents that the attending physician may advise.

The other two organisms are used mainly for the property they have of decomposing lactose (milk sugar), with the production of lactic acid.

The large bowel is one of the richest cultural environments for the growth of bacteria. There is constantly present abundant quantities of organisms, some harmful and some beneficial. In many individuals the putrefactive germs tend to predominate. When this condition takes place there is produced by these organisms various substances which, when absorbed and carried through the blood stream, act as poisons and produce the condition commonly known as auto-intoxication. The symptoms of the latter are manifested in many ways, and unless properly treated may lead to the development of more serious ailments.

The intimate relationship between putrefactive changes in the

alimentary canal and the disturbances of the important organs and in turn of the health in general is commonly recognized. The use of purgatives and chemical germicides or so-called intestinal antiseptics have proved ineffectual for getting rid of the bacteria that cause the production of the toxic substances. As Metchnikoff pointed out in his remarkable contribution to science in 1904: "Enough germs remained in the intestines to furnish abundant new cultures. The elimination of all new foods stopped new contaminations, but it was necessary to find some way to suppress the bacterial flora already existing from exercising harmful actions." Experimentation has revealed the fact that all the bacteria that produce lactic acid generally have the power of arresting the growth of bacteria which produce putrefaction. Metchinkoff recommended the use of the Bulgarian Bacillus to obtain the proper lactic acid content.

This organism, though having the power of producing large quantities of lactic acid, is in itself non-injurious to the human body. Experiments have revealed that the best procedure to adopt is to produce this inhibiting chemical (that is, the lactic acid), in the immediate environment of the putrefactive organisms that are to be destroyed: thus the use of the harmless micro-organisms in preference to the free acid itself.

The Bulgarian Bacillus mixed with starch or sugar of milk in tablet form, or, better still, Bulgarian Bacilli in a liquid culture medium, are employed. It is advisable that fresh cultures are used and these are to be preferred to the tablets. The fresher the cultures the more can one be assured of the efficiency which will be produced. The Bulgarian Bacillus produces exceedingly large amounts of lactic acid. The organisms survive and continue to live in the intestines for a long time after administration. It is claimed that they multiply rapidly in the intestines while producing these exceedingly large quantities of lactic acid. The latter hinders the growth of the harmful bacteria commonly found as the cause of intestinal fermentation and putrefaction.

The tablets can be employed but it is very important to be assured that they are fresh and are in turn kept at a cold temperature, as in an ice box, and renewed as per date on container. The same warning holds true for the liquid cultures, but generally the latter keep better than the tablets.

The Acidophilus Bacillus is an organism which is closely related to the Bulgarian Bacillus and has in recent years come into prominence.

This organism is one of the few acid-producing germs that appear to be a normal inhabitant of the intestinal tract of healthy infants. Experimentations have revealed that the bacterial content of the large intestines can be completely changed by feeding Bacillus Acidophilus. The latter becomes implanted in the large intestines, and because this organ is a suitable habitant, the organisms thus introduced flourish, multiply, and replace putrefactive and other injurious bacteria. The Acidophilus Bacillus itself is harmless, and during its development there are no poisonous by-products produced.

The Acidophilus Bacillus is sold either in tablet form or in liquid cultures as in the case of the Bulgarian Bacillus. In certain quarters there seems to be a demand created for Bulgarian and Acidophilus Bacilli. There are some manufacturers who have marketed the so-called B. A. tablets to meet this demand. The latter are tablets containing large quantities of the Bulgarian and Acidophilus Bacilli.

There are some investigators who have not only advised the administration of these lactic acid producing bacilli by mouth but also by enema.

In the second and third groups I include the many vaccines, therapeutic sera and antitoxins.

A vaccine, as the term is used today, is an infective agent so treated and modified as to prevent its power of multiplying and growing in the body. It is not, however, changed as to affect or prevent the production of specific protective substances when injected into the body.

The term vaccine has been misused and abused, not only by the layman but by some scientific and professional men as well. The former have, in some instances, misused this term in almost the same way that the term "drug" has been misused. The scientist refers to any remedial agent as a drug. This may or may not be habit-forming. Then why speak of drug "addicts"? Why not be specific and say "habit-forming drug addicts," "narcotic drug addicts," or, as advised and practiced by some people, the use of the slang term, "Dope," and say "dope addicts"? Why should one misuse

or abuse useful terms? In like manner the term vaccine has been applied erroneously to many products.

The term itself is derived from Vaccinia (from the Latin word meaning cows). Dr. Jenner first attempted to create a resistance against smallpox, by using the material from cows diseased with cowpox. The method of inoculation was later termed vaccination, and the material employed was called vaccine. Unfortunately the agent causing smallpox is still unknown. Though it is possible to prepare so-called smallpox vaccine, an effective remedy to be used to prevent smallpox, nevertheless the composition of this product is unknown. It may be said to be a modified unknown infective agent. The infective agent itself being poisonous is at times called a virus, then why not call the so-called smallpox vaccine, modified smallpox virus or as long as it is used to produce antibodies or specified protective substances, against smallpox, let it be termed anti-smallpox virus? In like manner, any modified unknown infective agent can be termed a modified virus, or anti-virus. Such terms would be descriptive of the products. The only other important preparation that falls in this class is so-called Rabies Vaccine, used to create a resistance against Hydrophobia. This can be properly termed Modified Rabies Virus or Anti-Rabies Virus, since the causative agent of Rabies or Hydrophobia is unknown.

There are certain preparations made by extracting the protein or albuminous matter from the pollen of various plants and grains. These are used as aids in the treatment of Hay Fever. For many years they were known as Hay Fever Vaccines. The proteins in the pollens are not necessarily the sole cause of Hay Fever, then why say Hay Fever Vaccine? Why not use the term actually descriptive of the product, Hay Fever Extract, or, better still, Pollen Extracts?

The term Vaccine is in most instances applied to what should be specifically termed "Bacterial Vaccines." A coined name, "Bacterin," has been applied to this class of products and in many ways is to be preferred.

A Bacterial Vaccine or a Bacterin is a suspension of dead or modified bacteria or products from the latter in a very weak salt solution to which there is generally added a preservative. The proper use of vaccines in the prevention of certain diseases is one of the most notable of triumphs of modern medicine. It was the

same Pasteur who revolutionized medicine by the introduction of the germ theory of disease who subsequently cleared the way for the investigation of the underlying causes of immunity and the introduction of the use of vaccines. In 1879, while working with the organisms which produce chicken cholera, he accidentally found how to modify these disease-producing germs so as to use them later in chickens, to create a resistance against this dreaded disease in fowls—Cholera. Pasteur found that germs possessing a high disease-inciting power became weakened as these organisms increased in age. When the latter, having lost their disease-inciting power, were injected, it was found that the fowl received the same disease but not in the fatal form, with the result that after recovery, the animal was able to withstand the attack of highly disease-inciting strains of the same organism.

Pasteur's original method had to be somewhat modified, inasmuch as it was more or less difficult to be always assured that the bacteria had been sufficiently weakened and that no living organism, especially in appreciable numbers, remained. Should a few living ones that possess a high disease-inciting power still survive, there is always a possibility of setting up a fatal disease, rather than a mild form to protect. Experiments soon revealed that dead bacteria and still better bacteria, which were so altered as to have lost their disease-inciting power, had the same power of causing one's system to produce protecting substances. It was found that such physiological alteration can be produced by low heat or by the application of a mild germicide.

Bacterial vaccines or Bacterins may be divided first into two distinct groups: autogenous and stock. The former are prepared from material obtained from the lesion or from the infected part of the individual into whom later the preparation is to be injected. Stock vaccines are those prepared from stock cultures kept in the laboratory. A simple Bacterial Vaccine is one made from only a single species of micro-organism. Mixed Bacterial Vaccines are those containing two or more different species of bacteria.

The first step in preparing vaccines is to obtain a culture medium most suitable for the growth of the organism or organisms from which the vaccine is to be prepared. A solid medium is generally employed, plain agar culture medium being satisfactory in many instances. The latter is a product prepared by adding agar,

a weed, to beef broth, which is a preparation made from meat and containing some inorganic and nitrogenous matter, the end product afterwards being sterilized. The agar, after being dissolved in the weak beef infusion, will cause the entire mixture to solidify upon cooling, thus giving a solid culture medium. This can be liquified if placed in a boiling water bath, but will solidify again when ordinary room temperature is reached. In culturing some organisms, it becomes necessary to fortify the plain agar medium with a natural fluid. For this purpose, blood, blood serum, and similar natural fluids are employed.

The culture of bacteria is then placed in an incubator at body temperature for twenty-four hours. At the end of this time the bacteria are procured by pouring a weak salt solution over the culture and gently shaking until all the micro-organisms have been suspended. The salt solution suspension of bacteria is then poured into a sterile container and shaken by some mechanical device or by hand so as to break up the clumps and make a uniform emulsion.

Bacterins are standardized by estimating the number of bacteria in the suspension. There are three methods commonly employed for estimating this number. The one worth mentioning at this time is the so-called Wright's Method. A small drop of the suspension of bacteria is mixed with an identical drop of blood. This is prepared for microscopic examination. We then can obtain a comparative ratio as to the number of bacteria and red blood cells present by actually counting the numbers of both. It is logical to assume that this proportion will be approximately the same in larger quantities as is found when a drop of each is compared. Knowing the approximate red blood cell content of a normal individual, by comparative proportion we can thus compute the amount of bacteria present in the suspension, after once establishing the ratio between the two. After the number of bacteria has been determined, the suspension is then diluted with a sterile weak salt solution so as to bring the content to any desired number per drop or per any given volume. The suspension is then sterilized by heat in a water bath at a minimum temperature and time of exposure that will kill the bacteria. This in most instances is 60° C. for one-half hour. A small quantity of a preservative is then added.

The Bacterial Vaccines are then subjected to purity and safety tests and placed in sterile containers. The greatest value of vac-

cines has been their application in the prevention of diseased conditions. Their use, generally in from three to twelve or more injections, given at intervals of at least a few days, and administered generally subcutaneously (that is, beneath the layers of the skin), is for the purpose of creating protective substances. By the presence of the latter the individual is in the position to counteract the effects of living organisms of the same type should they invade the system within a few months to a year after the period of vaccination.

If vaccination against Typhoid had not been carried out in the Great World War and had the same rate of infection prevailed as in the Spanish-American War, we should have had to each million men in the army the appalling number of 192,056 cases and 14,633 deaths from Typhoid Fever. It is hard to completely eradicate Typhoid Fever by sanitary methods alone, even though water, milk and foodstuffs as well as other sanitary measures are closely guarded. It is almost impossible to detect all Typhoid carriers as we do not always know of their existence. It is therefore apparent that Typhoid vaccination added to sanitary control would, if universally applied, go far towards making Typhoid Fever as uncommon as Smallpox. Many physicians in certain circles and sanitarians in general are attempting to popularize Typhoid vaccination. The advantages that would accrue warrant such a movement. You may at times hear of the so-called triple vaccine. This contains the Bacillus Typhosus, Bacillus Para Typhosus A and Bacillus Para Typhosus B. This so-called triple vaccine causes immunity not only against Typhoid Fever but also against Para Typhoid Fever, which, though uncommon in this area, is apt to be observed at frequent intervals in the southerly states and in certain sections of Europe.

Vaccines have also proven of value in the prevention of Asiatic Cholera and Bubonic Plague. They are being experimentally used with the hope of proving effective for the prevention of Pneumonia, Influenza, Meningitis, Whooping Cough, etc.

Vaccines have also been used for their curative value. For this purpose they have been extensively employed, especially in chronic diseased conditions, in which pus or some discharge is present, as in boils, pimples, carbuncles, chronic running ears and chronic running sores in other parts of the body and in chronic nose and throat trouble, etc. In many of the latter cases marked success has

been reported when these products have been employed judiciously. Many clinicians have recently been using vaccines even in acute conditions with varying degrees of success.

The Anti-Bacterial, Anti-Microbic or Therapeutic Sera are the sera (or the liquid portions) of the blood of animals in which there has been created a resistance against specific bacteria, the prepared sera in turn containing protective substances which are capable of counteracting the effects of these same organisms when living and active. In the preparation of these products, any animal can be employed. Horses are, however, commonly chosen for sera production inasmuch as they can be kept cleaner. They stand the injections and treatment better than other animals. Horse serum itself is less harmful than the sera of other animals. The cost of production is cheaper and from a commercial standpoint the yield of active serum is greater than would be produced in other animals.

The horses that are selected must be absolutely free from disease. They are given a thorough examination by a veterinary surgeon and kept under close observation for at least two weeks. During this time tests are made to insure freedom from glanders and tuberculosis. Some frequently practice the administration of a prophylactic dose of tetanus antitoxin, so as to create a temporary resistance against tetanus or lockjaw. No animal is retained unless found to be physically perfect. During the entire period that the horse is employed for the production of the sera, care is taken to be assured that they are constantly healthy and vigorous.

May I now explain briefly the manufacture of anti-Pneumococci sera used to counteract the effects of Pneumococci, which are the causative agents of most cases of Lobar Pneumonia. Just as the Anti-Pneumococci Sera are prepared, so are all other anti-bacterial sera prepared, with but very little variation.

Pneumococci are obtained from as many different sources as possible, in other words, the cultures that are used are ones which have been prepared from many different strains of the bacterium. The different individual strains are grown on cultures, and afterwards mixed together. These are then sterilized in a water bath at 60° C. for one-half hour. In other words, we practically start with a vaccine. The horses are usually infected with these dead or modified cultures for a period of from two to four months with increasing doses after each injection, depending

upon how the animal reacts. The injections are made under aseptic conditions subcutaneously (beneath the layers of the skin). The number of injections consist of from one to three per week. The intervals between injections vary, depending upon the susceptibility of these horses and the length of time necessary for the complete subsidence of the various symptoms which develop, *i. e.*, elevation of temperature, rigor, dejection (altogether commonly known as the reaction). At the end of the two to four month period, very small doses of the mixed strains of the same bacteriuu, that are alive and active, are given. Increasing doses at stated intervals are employed. At about the end of from six to eight months after the first injection was started, the animal is ready to be bled. So as to counteract the effects of the organisms, the horse develops in his system specific protective substances, generally termed antibodies. The production of the latter is in quantities and in excess of the needs at the time of the injection of the organisms. These antibodies or protective substances remain stored away for a period of time, and are ready to exert their influence against the organism for which they are specific. To bring out clearly what is meant when we say these protective substances or these antibodies are specific, may I say that Anti-Pneumococci Sera will only be efficient in counteracting the effects of Pneumococci and no other organism. Anti-anthrax sera will only be efficient in counteracting the effects in anthrax infections and have no effect in infections caused by other bacteria.

After a preliminary test, if the blood of the animal is found containing a high content of protective substance, the horse is ready to be bled. The animal is led into a specially constructed stall where the operation of bleeding is under perfect control. These stalls are in buildings of solid concrete and are separated from the stables and other buildings. The ceilings, walls, floors, and all compartments are constantly kept thoroughly aseptic. Apparatus, instruments and all equipment that are used here are thoroughly sterilized.

The animals are now washed with soap and water, their necks are shaved and asepsis is maintained by washing with an antiseptic solution and covering their entire body except the head and jugular vein with a sterile sheet or apron. A sterile cannula (a large needle), to one end of which is attached a sterile rubber tube, is

inserted into the jugular vein. The latter is at times made prominent by various means of compression or the skin surrounding the vein may be incised. The blood is allowed to flow through the rubber tube into high sterile glass cylinders which are protected by parchment covers. Anywhere from one to two gallons of blood can be obtained at one time without injuring the horse. In some instances, if the blood serum of the animal is found to still contain a high protective substance content, additional bleedings are repeated. If the antibody content is diminished, these horses can then be reinjected as previously described, so as to yield a high content of these specific protective substances.

The cylinders, containing the blood, are placed in refrigerators and the blood allowed to clot. After the clotting, the serum is collected in sterile containers in which there is placed some preservative. The sera are then filtered (if possible) through special filters to rid them of bacteria which may have accidentally gained entrance. They are then tested for sterility and toxic substances, and, if found satisfactory, they are placed in sterile containers as the anti-bacterial sera.

The composition of the complex bodies which are present as the valuable protective substances (acting as specific antibodies or therapeutic agents against the bacteria which produce them), is not known. On this account it has been almost impossible to isolate them or to remove the excess quantity of valueless and, in some instances, harmful blood serum. The methods of testing or actually determining their efficiency are numerous and vary in the different anti-bacterial sera. Unfortunately there is a lack of standardization, which we hope will be overcome in the near future.

The anti-bacterial sera are employed in the treatment of acute diseased conditions in which the causative agent has invaded all parts of our system. It is employed at a time when there is desired an immediate introduction of protective substances to counteract the effect of the invading organisms. The individual himself is either unable or time does not permit to wait for the production of these antibodies in his system, because of the seriousness of the condition. Therefore they are introduced after obtaining them from outside sources, in this case, the horse.

They are generally administered subcutaneously under the skin of the abdomen or between the scapulae. Injections into the vein

are employed in desperate or in the late stages of acute diseases. The only exception to this rule is in the use of anti-meningococcus serum. This is employed to counteract the effects of the meningococcus, the causative agent of epidemic Cerebro-Spinal Meningitis. This is administered directly into the spinal canal, removing first an amount of spinal fluid equivalent to the quantity of serum that is to be injected.

The following are the more important anti-bacterial sera that have been found beneficial, if employed as early as possible, and freely after the infection has been diagnosed: Anti-Anthrax Serum, used in the treatment of Anthrax in humans; Anti-Dysenteric Serum, found of value in reducing the mortality rate of bacillary dysentery; and Anti-Meningococcus Serum. The latter is probably the most successful of the different anti-bacterial sera. Anti-Pneumococcus Serum is of value as mentioned before.

Anti-Streptococcus Serum is used in infections throughout the entire system caused by the streptococcus. Versins Serum (anti-plague Serum), made from the bacillus pestis, the causative agent of plague, is most frequently employed as a preventative against plague. It is also of value in the treatment of this disease if used early.

All bacteria produce a poisonous principle, which is scientifically known as Toxin. In mose cases this toxin is held within the cell wall of the bacterium proper, to be liberated when the cell wall of the latter is broken up. A few of the disease-producing organisms, however, produce a toxin which is immediately thrown forth from the cell. This is known as an ecto, exo, or extra-cellular toxin. The diphtheria and tetanus bacilli, the causative agents of Diphtheria and Lockjaw respectively, are two of the commonly observed disease-producing organisms that produce extra-cellular toxins. It is due to the presence of the latter throughout the system rather than to the bacteria themselves that the symptoms common to Diphtheria and Tetanus or Lockjaw are produced. It is mainly to overcome and inactivate these extra-cellular toxins that the class of biological products known as antitoxins are employed.

The antitoxins are the true antitoxic bodies obtained from the serum of the blood of animals which have been immunized against specific known extra-cellular toxins. These antitoxic bodies are obtained from the serum, dissolved in a weak salt solution, filtered, and a preservative is added. After standardizing them, tests are

performed to insure their purity. They are then placed in sterile syringes or containers ready for use.

In the preparation of antitoxin, horses are employed. All precautions as observed when these animals are used for the production of anti-bacterial sera are taken here. Instead of injecting the horses with bacteria, the injections are made with the extra-cellular or the true soluble toxins of the bacteria. I call your attention specifically to the production of Diphtheria antitoxin. Tetanus and other antitoxins are manufactured in like manner with little variations.

A culture of the Diphtheria bacillus is selected which is found by observation to produce a large amount of a powerful extra-cellular or soluble toxin. The organism is usually obtained originally from patients suffering from Diphtheria. The latter is cultivated on suitable solid culture media and when kept on hand is known as the "Mother Culture." When needed for the preparation of antitoxin, some of the organisms from the latter are replanted on an additional media and kept in an incubator at body temperature for twenty-four hours. These known as "seed cultures" are therefore employed for the planting of the organism into sterile flasks containing large quantities of sterile veal broth. The latter are placed in compartments or incubators kept at body temperature, for a period of from six to eight days. Within this time, the Diphtheria bacillus is constantly multiplying, giving off large quantities of extra-cellular toxin, which, being soluble, goes into solution. The cultures are then usually examined, and, if found pure or free from contamination, an antiseptic is added and the mixture is also allowed to stand for twenty-four hours. The bacteria are killed by this procedure. They are then filtered out and the clear filtrate containing the soluble toxin is stored away protected from the action of heat and light, until required for use.

Having obtained fit horses and having determined by tests the fact that the toxin is active, the development of the antitoxin can then be started. Due to the susceptibility noted in various horses, the first doses of soluble toxin which are administered are very small or otherwise reduced in strength by slightly heating, adding an antiseptic, or combining it with antitoxin and gradually withdrawing the latter, as the injections are continued until pure toxin only is injected.

The injections are made under aseptic conditions beneath the skin in the flank region. From one to three injections are given every week, each injection consisting of gradually increased doses. The intervals between injections depend upon the susceptibility of the horses or the subsidence of any reaction that may develop.

So as to counteract the effects of toxin, the horse develops in his system specific substances which will counteract or neutralize this toxin. These protective substances being specific for toxin are called antitoxin or antitoxic bodies. The antitoxin content of the blood increases with increased doses of toxin, until such a point or level which is reached by each animal when the antitoxin contents remain stationary and are not followed by further increase, even though the injections with toxin are continued. This level is determined in each animal by obtaining a small quantity of blood from time to time, beginning usually from six to eight weeks after the first injection.

The strength of antitoxin and the length of time required to produce a maximum yield of the latter will vary greatly in each animal due to susceptibility. At times it happens that some horses which have been treated with injections for long periods of time will yield a serum of so low an antitoxin content, as not to warrant the use of such animal, as the resultant product is only of little commercial value.

At the end of the period when a maximum yield is produced, which on an average is from three to four months after the first injection, the horse is bled. The bleeding is conducted in an almost identical manner as explained previously in the manufacture of antibacterial sera.

The blood is allowed to pass into large vessels containing chemical solutions which prevent the blood from clotting. The liquid portion is then treated by various procedures in which the true antitoxic bodies are finally obtained. These are purified, dissolved in a weak salt solution, filtered and standardized. A preservative is added and they are then placed in suitable containers ready to be used.

Diphtheria antitoxin is used both as a remedial and a prophylactic agent. It has been found a specific in the treatment of Diphtheria. It is usually administered hypodermically or intramuscularly. In advanced cases, when immediate relief is required,

it is given intravenously. Administration during the early stages of the disease, when the symptoms just appear, is always to be practiced, as the more time that elapses before the antitoxin is injected, the less chance will there be for a prompt or hasty recovery. Large doses are generally administered so as to be assured of an antitoxin in excess of the poisonous toxin. An excess of the former will never produce harmful results.

Diphtheria antitoxin is a valuable prophylactic agent. It should be administered to all who have been exposed to infection with Diphtheria. It should, however, be stated here that this protection lasts for not more than two to three weeks. Within recent date mixtures of Diphtheria toxin and antitoxin have been marketed and used as a more valuable prophylactic agent than Diphtheria antitoxin alone. Generally three doses are given, the later doses containing more of the toxin and less of the antitoxin. This treatment is being employed successfully to create a more lasting protection against Diphtheria in children or in adults, who are more apt to be found in an environment where Diphtheria is common.

The Tetanus bacillus is widely distributed in nature. The chances of Tetanus or Lockjaw setting in are numerous, especially when an injury has caused deep, lacerated wounds in which considerable tissue destruction was produced, and in which foreign particles have become imbedded.

Under all such conditions, it is imperative that tetanus antitoxin should be administered so that the antitoxin may neutralize any toxin that may begin to form. If the toxin is allowed to develop, it quickly invades the motor nerve cells, forming a combination or union which the antitoxin cannot break up. The greatest value, therefore, of tetanus antitoxin is as a prophylactic agent. Tetanus antitoxin administered immediately after infection or after early symptoms set in will quickly neutralize the soluble toxin before it reaches the motor nerve cells, thus preventing a strong union.

Other antitoxins have been prepared from the soluble toxins from other organisms. The latter have thus far been found to possess but slight curative values.

Another class of preparations which you may hear of is the so-called "Sensitized Bacterial Vaccines" or "Sero-Bacterins." The latter are prepared in the same manner as the bacterial vaccines or bacterins, but differ in the following additional steps:

After the bacterial suspension has been thoroughly emulsified and the number of bacteria determined, a portion of the serum of an animal (that had been immunized against the same species of bacteria as found in the suspension), is added. The mixture is allowed to stand for twenty-four hours in an incubator at body temperature, with occasional agitation. At the end of this time, the mixture is centrifugalized and the supernatant liquid (consisting of the weak salt solution and serum), is discarded. The remaining bacteria are then washed and again suspended in a weak salt solution. After a preservative is added, the preparation is treated in like manner as are the plain bacterial vaccines or bacterins.

The treatment with anti-bacterial sera is said to sensitize the bacteria so that they are more easily attacked by the forces in the patient's system.

The sero-bacterins are found to be more rapid in their production of protective substances. They usually minimize undesirable reactions. Larger doses of sensitized bacterial vaccines at more frequent intervals can thus be given.

Sensitized Bacterial Vaccines of practically most of the bacteria (from which plain bacterial vaccines are prepared), are marketed.

Many preparations made from bacteria or products from the latter are available and are being employed as aids to assist in the diagnosis of certain conditions. We have the so-called "Tuberculins." The latter are either modified tubercle bacilli in suspensions or products from the latter. They are really closely related to the bacterial vaccines. Tuberculin is of greatest value as a diagnostic agent in tuberculosis.

Preparations similar to some of the tuberculins have resulted in the introduction of the products used in the so-called Mallein and Luetin tests. The former is a test used to detect the presence of glanders, especially in animals other than humans. The Luetin test is said to be of some slight value as an aid in the detection of syphilis, during certain stages of this disease.

Most of the tests that are employed as diagnostic aids are skin tests. The preparation applied upon, beneath or between the layers of the skin is allowed to react. During such intervals the patient is held under close observation, both as to physical symptoms in general and as to the appearance of the area surrounding the site or point of injection.

One other test worth mentioning is the "Schick Test," a skin test employed to see if one naturally possesses a resistance against Diphtheria. The preparation employed to perform this test is nothing more than a solution of the true soluble toxin from the Diphtheria bacillus.

I will finish the talk this evening in explaining to you the manufacture of modified Smallpox virus and a brief consideration of Smallpox vaccination.

The product used as a prophylactic against Smallpox is not an anti-microbic serum, nor a toxin or antitoxin, and not even a true bacterin. Its exact composition is a mystery due to the fact that the agent causing Smallpox is unknown. Inasmuch as the latter is of a poisonous nature, the term "Virus" (meaning poisonous matter) has been applied to it. Smallpox Virus (after attenuation) is the product used to create a resistance against smallpox, a disease which killed so many humans in days gone by and which is at present causing some concern to health authorities throughout the country. It is therefore advisable that this preparation should be called "Modified" or "Attenuated" or "Anti-Smallpox Virus."

Young calves (heifers, from three to six months, weighing about 200 pounds), are selected. They are kept in quarantine for about two weeks, during which time they are given rigid inspection by competent veterinarians and also tested for tuberculosis by means of tuberculin.

The calves are well fed (usually with milk) and kept under conditions as sanitary as it is possible to keep them (usually in cemented buildings, free from straw, dirt, etc., and which are washed at frequent intervals).

They are transferred to a room where the hair is clipped from the entire body. They are then scrubbed with an antiseptic solution and bathed in sterile water. They are finally removed to other quarters, shaved, and brought into the operating room for vaccination.

During the operation, every aseptic precaution is taken. The heifer is strapped securely to a specially prepared table, back down, and the exposed abdomen and inner surface of the flanks are scrubbed, shaved again (if necessary), disinfected and finally washed with several portions of sterile water. Then, with a sharp scalpel,

longitudinal incisions are made, taking care that no blood is drawn. A previously prepared virus (to which glycerin has been added) is thoroughly rubbed in. The virus, which has been subjected to rigid tests to insure purity and has been found of a high potency, is usually kept for vaccination purposes and known as the "Seed Virus."

After the inoculated material has been absorbed, the animal is removed to his quarters, where the greatest aseptic precautions are exercised to protect all vaccinated areas from contamination. At the end of from six to nine days (which time is known as the "propagation period"), pustules form along the line of scarification, in which the virus is found.

At the end of this period the heifer is again brought into the operating room, strapped on the table and generally bled to death. The vaccinated area is repeatedly washed with sterile water, so as to remove all crusts or scabs about to form, thus leaving the area covered with rows of pearly white vesicles. By means of a special instrument, the pustular material or lymph (known as "Vaccine Pulp") is removed and placed in sterile glass containers.

A thorough postmortem is conducted, and if the carcass (dead heifer) is found to be slightly abnormal from a health standpoint, the so-called vaccine pulp is destroyed and thrown away. If the animal has been found perfectly fit, thus confirming the physical and clinical examination, the pulp is mixed with proper proportions of glycerin and sterile distilled water and transferred to a specially constructed room, where it is ground into a uniform emulsion in a special grinding apparatus. It is then placed in a refrigerator, remaining here for a period of from three months to a year. During this time, all bacteria (which may get in even after observing all aseptic precautions), are destroyed or so modified that they are unable to produce disease.

After determining its activity, safety and purity tests are conducted. If found satisfactory, it is marketed in hermetically sealed aseptic capillary tubes, known most frequently as points.

All biological products are to be kept in a dark, cool place if it is desired that they retain their activity for any length of time. The potency of modified Smallpox Virus, more so than any other of

the products mentioned, is easily influenced by the variancy in temperatures.

Smallpox prevailed in all countries for many centuries. It was one of the most fatal diseases known, the average death rate in epidemics being close to 60 per cent.

Inoculation as a means of checking the spread of epidemics was practiced by the Chinese centuries before the Christian era. It consisted in the artificial transfer of the Smallpox virus by rubbing the scabs from a diseased patient into the skin of the one to be immunized. This usually resulted in a mild case of Smallpox, a quick recovery, and a lasting immunity. This same practice was later employed in Europe, but after a time it was observed that the disease itself was spread in this way and to this procedure is accredited the spread of many of the fatal epidemics.

Dr. Jenner was the first one to study this problem scientifically and in turn succeeded in artificially immunizing individuals. He observed the close relationship between a disease of cattle known as Cowpox, and Smallpox in man.

The practice today consists in introducing the modified Cowpox virus from cattle into man, thus doing away with the inoculation from scabs of human cases, where there is not only danger in the spread of Smallpox, but also the possibility of the spread of other diseases.

After extensive investigations, numerous workers have definitely proven that Tetanus or Lockjaw is not caused by vaccination against Smallpox. If infection with Tetanus does set in, it is not due to the Smallpox virus, but due to the contamination of the vaccination wound by the patient or other persons, such as may occur in the infection of any other wound which may not be properly cared for.

The vaccination of the human being is performed by slightly scarifying the skin of the arm or leg with a lancet, needle, or other scarifier and rubbing into this area by means of the sterile glass point an active modified virus. It is to be remembered that the resistance which is created does not last forever. The immunity lasts for about seven years and rarely over a period greater than ten years. A revaccination is important so as to receive again an identical benefit as obtained from the first vaccination.

SOME NOTES ON CHLORAMINE T.

By W. V. Kopfstein.

The many admirable qualities of Chloramine T are indicated by the widespread interest of the medical profession, its use by the laity as a general antiseptic and germicide, and its increasing volume of production.

In my contact with manufacturers of Chloramine T tablets I have found the same general difficulties which naturally resulted from the use of a product of recent discovery. Nothing was known of the proper methods of handling, compatibilities with other chemicals, effects of heat, light, etc., upon Chloramine T. It is therefore hoped that the following data will be of some assistance to any manufacturer who is having difficulties with the tableting of Chloramine T.

It has been shown (*) that Chloramine T in dry crystalline form which has a purity of 96-98% and perfect solubility can be produced without burdening the manufacturer. This purity is figured on the chlorine content of the product and on a dry basis. In such a product we should find a water content of 18-20% and a chlorine content of 12.25-13.00% and as stated above perfect solubility in water. It has also been shown that the stability of the product itself is contingent upon its purity and that with a product of the above specifications we have a Chloramine T which is not only stable in dry crystalline form but also in water solutions and in solutions which contain NaCl, $NaHCO_3$, Na_2CO_3.

Furthermore, I have shown in a paper published privately and used for advertising purposes that Sodium Chloride, Sodium Bicarbonate, Sodium Carbonate, Soluble Starch, Sodium and Potassium Tartrate, Sodium Borate, Zinc Stearate, Soluble Saccharin and purified Talc are all compatible with Chloramine T. All acid fumes, chemicals of an acid nature, ammonia fumes, Glycerine,[1] Sodium Citrate, Boric Acid, Sugar, Ammonium Chloride, Insoluble Saccharin, Soluble Soap and Alcohol are incompatible with Chloramine T.

*J. Bebie: *Journal of American Pharmaceutical Association*, Vol. IX, No. 10, October, 1920.

[1] J. Bebie: *Ibid.*

If, therefore, the tablet manufacturer receives a product of the specifications outlined above, there should be no great difficulty in producing good tablets from Chloramine T. It must be admitted that before the manufacture of Chloramine T was thoroughly understood the intermediates from which it was made often contained Ammonium Salts which were not entirely eradicated. Slight amounts of these impurities remaining in the finished product no doubt had some influence on the stability of the early manufactured Chloramine T. With the added experience and proper control in the course of manufacture the above cause for decomposition can be wholly eliminated.

The great majority of manufacturers of Chloramine T tablets have passed at one time or another through the same difficulties. The difficulties were, in order of their importance, decomposition, capping and picking and difficulties in getting a good granulation.

Decomposition in most cases has been relatively slow, the tablets turning yellow and pasty or finally melting to a yellow pasty mass. At other times, and especially in the very hot summer months, the decomposition has been spontaneous and with explosive force.

Chloramine T may well be placed in the delicate group of products from which tablets are manufactured. The list of incompatibles given above will bear out this statement. Contamination from any source must be guarded against and the worker and his implements must at all times be scrupulously clean. Not only this but the atmosphere in which the tablets are made and dried must be free from ammonia and acid fumes, alcohol fumes, creosotic odors, etc., and the temperature at which the product is dried must not in any case exceed 100° F.

The prime consideration in the manufacture of any tablet is to present the chemical in as near its original form as it is possible to do. Yet it is strange how many manufacturers of Chloramine T tablets have tried to add different excipients for one reason or another. In some cases the practice of economy entailed the use of a die the size of which necessitated the addition of some excipient in order to completely fill it. The favorite substance for this purpose seemed to be sugar. The usual loss through decomposition from this cause was generally more than the outlay for a new die would have

been. Another reason for the addition of excipients was the wish to combine the antiseptic properties of other chemicals with that of Chloramine T. In all cases some substance which was incompatible with Chloramine T was chosen, thus causing decomposition sooner or later.

It has been known from the time of its discovery that Chloramine T in a moist state must not be brought into contact with metals of any kind. By a moist state we mean when more water than the water of crystallization is present. Yet where granulation has been carried on it has invariably been the case that a brass or copper screen has been used with moist Chloramine T. Trouble from this source can easily be overcome by bakeliteing the wire of the screen which is used. Care should be used to rebakelite any portion of the wire which may peel through use or corrosion of the metal itself.

It is a question whether the shape of the tablet has anything to do with capping or picking. Some manufacturers claim that a flat shaped tablet has less tendency to cap while others claim the same for the tablet with the curved surface. A careful adjustment of the pressure, however, will overcome this difficulty. The use of talc as a lubricant is objectionable by the fact that it will appear that the tablets are not perfectly soluble. Neutral petroleum oil has been found not to decompose Chloramine T, so that it could be used as a lubricant also.

Another important feature to be considered is the quickness with which the tablet will disintegrate. There is no doubt but that a hand moulded tablet of Chloramine T is far superior to the machine compressed tablet in this property. An ordinary hard rubber mould does very well for this work and no granulation is necessary but merely moistening the product so that it will cohere in the mould. The disadvantage of this method of tableting is the amount of labor entailed.

In this connection it seems strange that no manufacturer has attempted to market Chloramine T in capsules. A No. 1 gelatine capsule will hold 4.6 grains, which is the usual amount of Chloramine T in the tablets on the market. There would seem to be certain advantages in this method of marketing Chloramine T. The

product would need no granulation or addition of excipient. It could be packaged otherwise than in bottles and at the same time would be free from the decomposing effects of various fumes. Chloramine put up in capsules has remained stable for a period of two years and probably will remain so indefinitely. As for quickness of solubility there is nothing to be desired. The capsule is separated and the contents dropped into water with complete solution in twenty to thirty seconds.

In summing up it has been found that the successful tableting of Chloramine T has been achieved by the adherence to the few simple rules which follow.

Use as little excipient as possible and then only such substances as are perfectly compatible with Chloramine T.

Granulation is not entirely necessary. In some cases flake crystals which are in themselves slippery will work very well for tableting, flowing easily in the machine. The best results have been obtained in using the material as it comes from the producer (100% passing a 20 mesh sieve). For hand moulded tablets the material must be moistened so that it will take and hold the shape of the mould.

Capping and picking can be entirely overcome by the correct adjustment of pressure. In very exceptional cases the use of neutral petroleum oil as a lubricant can be advised.

In working up the Chloramine T into tablets and when drying the tablets, be sure the atmosphere is free from acid and ammonia fumes and odors such as creosote, etc. The temperature for drying should not at any time be above 100° F. since above this temperature decomposition is likely to set in, especially if the water of crystallization is driven off. If the tablets have a tendency to turn yellow it is a sure indication that decomposition has started or will ultimately set in.

WM. V. KOPFSTEIN.

December 18, 1922.
Webster Groves,
Missouri.

EFFICIENCY OF SOME COMMON ANTI-FERMENTS.

Part II.

Ellery H. Harvey.

Utilizing the method described in Part I * the relative value of anti-ferments as measured by the retarding action they exert on the hydrolysis of sugar-yeast solutions has been further studied and the list extended to include many of those now in common use. Additional experience with the method emphasizes the importance of exercising the care common to all quantitative determinations with particular emphasis upon the quality and quantity of the yeast used. When any set of comparisons are made at one time, using the same yeast solution, the results are strictly relative; if duplicate determinations are made from time to time a standard yeast must be used or one set of results will not compare exactly with any other set due to the variability in moisture content, age, weight, filler, etc., of commercial yeasts bought on the market.

The efficiency of the anti-ferments used in food preservation as shown by this method is confirmed in actual practice by the relative frequency with which the several anti-ferments are used. Saccharin, in addition to its intense sweetening power, has some anti-fermentative action, although the quoted statement of Squibb [1] that it has "about the same power as boric acid as an anti-ferment" is not borne out by this method of testing. In the several instances of incomplete solubility of the anti-ferment the results are probably slightly low. Finding an anti-ferment low in efficiency at this concentration obviously does not preclude satisfactory results in preparations in which larger amounts are not objectionable.

Effect of Various Anti-Ferments on Yeast Activity.

The results tabulated below were obtained by adding 5 cc. of a 1% solution of the anti-ferment to 50 cc. of a sugar solution (made by dissolving 114.4 gms. of sugar in distilled water sufficient to make 1000 cc.) in which 12 gms. of yeast had been dissolved. A temperature of 23° C. was maintained. Readings were made in a 100 mm. tube, after filtration, in terms of the International Sugar Scale. Original reading 20.0.

**Amer. Jour. Pharm.*, Vol. 94, No. 12, December, 1922.

[1] Leach: *Food Inspection and Analysis*, 3d Ed., page 851.

Chemical	1st hour	2d hour	3d hour	4th hour	5th hour	6th hour	7th hour	8th hour	Remarks
Nitro-benzol	14.7	11.9	10.0	8.6	7.3	6.7	6.4	6.1	Technical
Boric acid	14.8	12.3	10.0	8.7	7.5	6.8	6.4	6.1	U. S. P.
Oxalic acid	15.3	13.6	11.9	10.2	8.6	7.5	6.6	5.7	Commercial
Abrastol	15.1	12.7	10.4	8.7	6.9	6.1	5.4	4.9	Partially insol.
Sodium hydro-sulphite	14.6	11.3	8.9	7.4	6.0	5.4	5.0	4.7	Technical
Oil of Birch	18.2	16.2	14.1	12.3	10.2	8.1	6.0	4.1	Natural
Saccharin	14.6	12.3	10.0	7.8	6.5	5.7	4.9	4.0	U. S. P. soluble
Oil of Cloves	18.1	15.8	13.7	11.6	9.5	7.4	5.4	3.9	Commercial
Oil of Sassafras	18.2	16.0	13.7	11.6	9.5	7.4	5.3	3.7	Natural
Sodium fluoride	15.1	12.4	10.3	8.5	6.9	5.7	4.6	3.6	Technical Sl. insol.
Beta-naphthol	13.1	10.5	8.2	6.5	4.9	3.9	3.2	2.7	Not completely soluble
None	15.5	11.3	8.2	6.0	4.4	3.1	1.9	0.9	

Effect of Salt on Yeast Activity.

While not an anti-ferment in small quantities, the extensive use of salt in the preservation of foods made it desirable to determine what effect it had on yeast activity. In 50 cc. portions of the sugar-yeast solution described above, dry salt of table grade was dissolved and readings taken hourly at 23° C. in a 100 mm. tube, after filtration. Original reading 20.0.

The data reveals that yeast activity is but slightly inhibited by dilute salt solutions and is fairly rapid even in higher concentrations.

Per cent. of Salt	1st hour	2d hour	3d hour	4th hour	5th hour	6th hour	7th hour	8th hour
None	15.5	11.3	8.2	6.0	4.4	3.1	1.9	0.9
5	15.8	12.9	10.3	8.0	5.7	4.0	2.7	1.8
10	15.9	13.3	11.0	9.0	7.2	5.7	4.6	4.0
15	16.0	13.4	11.5	9.7	8.2	7.1	6.4	6.0
20	16.1	13.5	12.1	10.8	9.9	9.2	8.3	7.7
25	16.3	13.8	12.3	11.0	10.3	9.8	9.4	9.0

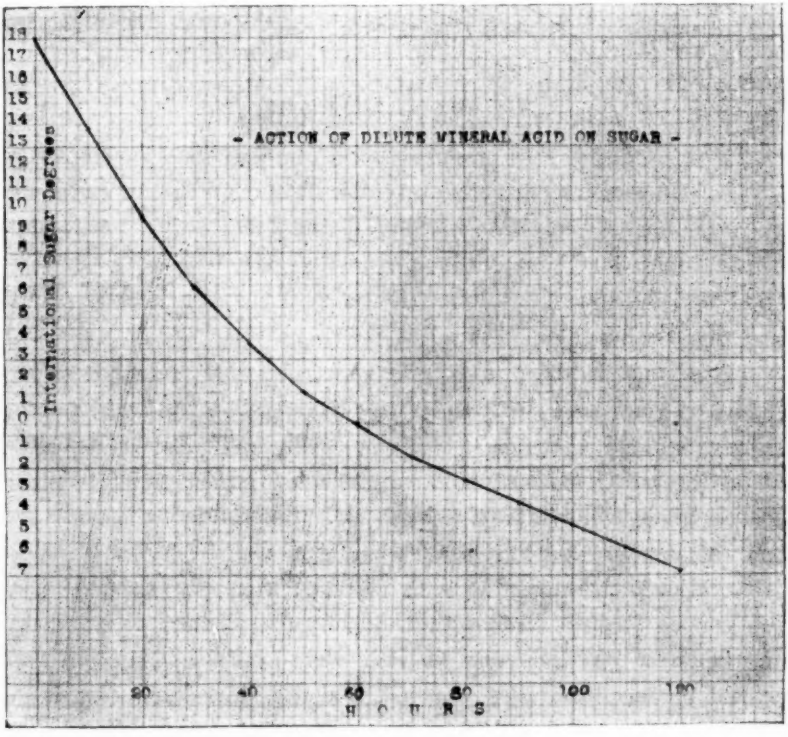
Effect of Dilute Mineral Acid on Sugar.

In common with enzymes, mineral acids invert sugar to equal parts of dextrose and levulose. For purposes of comparison the action of dilute hydrochloric acid at 23° C. is tabulated below.

25 cc. N HCl were added to 275 cc. of distilled water. In 100 cc. of this solution 10 gms. of sugar were dissolved and read-

ings taken at ten-hour intervals. The general similarity between enzyme-inverted sugar solutions and acid-inverted sugar solutions indicate a similarity in action, probably catalytic in nature.

Original	+18.0
End of 10 hrs.	+13.8
End of 20 hrs.	+9.7
End of 30 hrs.	+6.4
End of 40 hrs.	+3.7
End of 50 hrs.	+1.5
End of 60 hrs.	0.0
End of 70 hrs.	—1.5
End of 80 hrs.	—2.6
End of 90 hrs.	—3.7
End of 100 hrs.	—4.7
End of 110 hrs.	—5.8
End of 120 hrs.	—6.8



ACTION OF DILUTE MINERAL ACID ON SUGAR.

Conclusions.

1. The use of the volatile oils of spices, within the limits set by the taste, is an aid in the preservation of such food products as catsup, tomato sauces, etc.

2. Yeast is quite tolerant of salt solutions.

3. Saccharin exerts a mild anti-fermentative action, the quantity permissible in use being regulated by the taste.

4. Dilute acid hydrolysis of sugar at room temperature gives data, which on plotting, produces a curve having the characteristics of enzyme-inverted sugar solutions.

BEHAVIOR OF SOME CRUDE VEGETABLE OILS WITH COPPER ACETATE.

By W. H. Dickhart.*

It is well known to pharmaceutical chemists that copper acetate is used to detect colophony in asafetida. Thus, we find in Kraemer's *Scientific and Applied Pharmacognosy* the following: "A petroleum benzin solution (of asafetida) should not give a bluish green color upon shaking it with a solution (1 in 20) of copper acetate (detection of colophony)."

Applying this test to crude vegetable oils, we find various shades of green are produced in the petroleum benzin layer, ranging from pale light green to a dark emerald, with all the important crude vegetable oils except cottonseed oil. On the other hand, no color is given by any of the refined oils. The following list of crude and refined oils were tested by shaking a solution of 10 cc. of oil in 10 cc. of petroleum ether with 10 cc. of a freshly prepared (1 in 20) copper acetate solution and allowing the mixture to stand several minutes. Where crude oils only were available, these oils were refined by the usual alkali method, and the refined oils tested.

*New York Produce Exchange.

Crude Oils.			*Refined.*
Cottonseed	(green color)	negative	negative
Cocoanut	"	positive	"
Corn	"	"	"
Castor	"	"	"
Chinawood	"	"	"
Kapok	"	"	"
Lumbang	"	"	"
Linseed	"	"	"
Olive	"	"	"
Palm	"	"	"
Palm Kernel	"	"	"
Peanut	"	"	"
Perilla	"	"	"
Rapeseed	"	"	"
Sesame	"	"	"
Soya Bean	"	"	"
Tobaccoseed	"	"	"
Teaseed	"	"	"

This test furnishes a means of differentiating without further analysis between crude Kapok and crude cottonseed oils and can also be used to detect as small amount as one-half of 1 per cent. of any crude vegetable oil in crude cottonseed oil by the following modification of the above method.

Wash ten grams of crude vegetable oil into a 250 cc. glass stoppered graduated cylinder with 150 cc. of petroleum ether and shake vigorously with 40 cc. of the copper acetate solution, permit the aqueous solution to settle, filter the petroleum ether solution into a 4 oz. cut glass oil bottle, place the bottle into the Lovibond tintometer and compare the color with a blank that was made at the same time in the same way and containing only pure crude cottonseed oil. A crude cottonseed oil containing 1 per cent. of other vegetable oils, such as palm, cocoanut, etc., tested by this method, gave a very distinct green color, so pronounced when compared in the tintometer with the blank containing pure cottonseed oil, that there could be no question of the contamination.

The color in the petroleum ether, resulting from the action of the acetate upon the crude oil, appears to be colloidal in character, since it will pass through ordinary filter paper, but is completely held back by parchment, the filtrate containing none of the color. By evaporating the petroleum ether from the filtrate, the original crude oil was recovered and showed no green color.

AN EXAMINATION OF RODILLON'S TEST FOR NITRITES.

By Henry Leffmann.

The presence of nitrites in water is generally regarded as an indication of pollution, and several tests for them have been devised. As the amount present even in highly polluted samples is quite small, only delicate tests are available. A test that was long in use and has real value is with starch solution, potassium iodide and hydrochloric acid. In the presence of nitrites the blue starch-iodine combination is produced. Solution of 1-3 diaminobenzene with hydrochloric acid is frequently used, but the most delicate test is with a mixture of alpha-aminonaphthalene and sulphanilic acid, both previously dissolved in strong acetic acid. In the presence of even very minute amounts of nitrites, a pink solution is produced.

Recently, G. Rodillon described (*Ann. Chim. Phys.* [7], 1922, v. 26, 376) a test with a solution of 3 grams of resorcinol in 50 grams of "pure" sulphuric acid. The resorcinol should be practically colorless. The reagent is used by underlaying a portion of the sample in a test-tube. In a few minutes a colored ring appears at the point of junction. The author does not give any explanation as to what changes take place when the resorcinol is mixed with acid, nor the effect of the reagent on the nitrites present. The action of strong sulphuric acid on resorcinol was studied by Piccard and Humbert (*Ber.*, 1876, IX, 1479). They found that, under ordinary conditions, if 1 part by weight of latter is mixed with 4 parts of the former, a di-sulphonic acid is produced, which separates as a crystalline mass, which is freely soluble in water and practically insoluble in sulphuric acid. Owing to the possibility of several isomeric forms, it is probable that the result of the action is different at different temperatures and with different proportions of the two substances. The phenol-sulphuric mixture which has long been used in determining nitrates in water was at first believed to be mostly 1-4 phenolsulphonic acid, but later investigations showed the reaction to be more complex, di-sulphonic acid being formed. The designation of the acid as "pure" cannot be understood as prescribing anything but the concentrated substance. Rodillon states that the reagent is a clear, greenish yellow liquid and that

it keeps well. It seemed possible that the prescription for 50 grams might be a misprint for 50 cc. and solutions were made up in both proportions. Even the smallest ratio of the acid is far above the amount required for complete sulphonation, hence a considerable excess will remain. Both proportions gave a solid crystalline mass. The smaller proportion acted much more slowly than the larger, requiring to stand over night before the solidification occurred, but when once crystallized both mixtures did not melt in boiling water.

The test, as noted above, is made by underlaying the sample with about 2 cc. of the reagent. A convenient volume, say 10 cc., is poured into a test tubs and the reagent passed down along the side of the tube. It is not possible to do this with the reagent cold, and if heated until liquid it acts violently when introduced into the test tube. Under any circumstances, underlaying tests are only trustworthy in qualitative work, and the available tests for nitrites are so delicate, convenient and accurate that it is not likely that the resorcinol test will receive general acceptance. The presence of nitrites in natural waters is generally regarded as evidence of pollution of a serious nature, but it must not be overlooked that they may be present in deep (artesian) waters without having any special sanitary significance. Nitrites are very poisonous, but the amounts existing in natural waters are always far too small to deserve consideration from that point of view.

ABSTRACTED AND REPRINTED ARTICLES

THE PASSING OF THE COUNTRY DOCTOR.*

"Sometimes He Cured, Often He Relieved, Always He Comforted."

Ivor Griffith, Ph. M., Philadelphia, Pa.

A lonely road leading into gloomy hills; a dreary, unpromising road that offers but little joy to the weary traveler who would plod its uneven way to reach his destination. A bleak landscape robbed by chill November of all its charms of other days. Rain, cold rain, beating, drizzling rain, that seeps and soaks and permeates through

*Reprinted from *The Eclectic Medical Journal.*

every known protection. And over the sodden road, swinging from rut to puddle, rolls an old-fashioned four-wheeled buggy, drawn by a tired horse.

The animal, weary with lifting its weighted hoofs out of the gummy mire, wanders along with an enduring patience and dangling reins that rarely jerk to tightness, tell the story of the driver's total trust in good old Dobbin's judgment. Behind the black oiled canvas that drapes over the front of the carriage sits the driver, the country doctor, silent in contemplation, and changing his posture only rarely and then to ease a tired muscle or soothe an aching joint. The whinnying winds blow bulging pockets in the carriage coverings, and tall cedars, lone sentinels of plebeian boulevards, grudgingly sway their tips in the swirling air currents, as over the bending roads these children of the storm pursue their tedious mission.

Soon they come to the foot of the hills, where lack of timber tells the tale of a hardy pioneer's clearing. And just below the timber-line is the end of the journey, the little cabin whence came the call that brought the doctor to his duty. The buggy stops under a covered shed, and the master of Dobbin steps down, ties his faithful steed to a hitching post, and walks on toward the lowly cabin. In his hand he carries a small leather case, his "vade mecum" in emergency, laden with precious balms and healing lotions. In it are little vials filled wth murky concentrations, potent antagonists of human dissolution, pellets and pills fashioned in a pharmacy and designed from an expansive materia medica. The bowels of the earth, where the minerals lie, and plants that grow upon its face; animals that roam the green fields, and the creatures that creep upon the unploughed wilderness, all have contributed to this small store of healing agents, the contents of the little black grip. Aloes from darkest Africa; India's choicest poppy juice; essence of the Jesuit bark from hot Peru; gums and aromatic oils from Arabia; bitter rhubarb from China land; herbs and leaves from the little Emerald Isle; mellow oils from sunny France; made up mulls from German mills; the wealth of America's drugs—all of these and more are in the little vials and bottles that comprise the fighting armamentarium of the honest old doctor of the countryside.

Follow him into the cabin. Waiting for his coming is the mother; mother of the hillside cabin; mother of the better America; mother of men who have come from the mountains to mould the destinies of

a great nation; mother of men who have come with the abiding strength of the cedars and the sturdy reliance of the great oaks to lead their nation to pinnacles of liberty and to the feet of God; mother of Lincoln, of Garfield—that is the mother of the cabin at the foot of the hills.

And waiting at the door for his coming is this mother, whose first born child is ailing, the child whose racking pains he comes to quiet or mitigate. The lines of her loving face, the eager, hopeful stare of her tired eyes give mute testimony to a long and loyal vigil at the bedside of the little sufferer. Her tale of the patient's plight is soon unfolded, and the doctor goes on to the bedside, where the anxious, care-worn father, son of the soil, also keeps his vigil. The father rises and greets the doctor with the customary respectful silent handshake and retires to the shadows to watch with hopeful eyes the man who brings confidence back to his heart, and assurance that Death shall not come by his threshold to claim the first-born son. Upon the humble cot lies the troubled infant, sick almost unto death. His little Cupid face, that but yesterday gleamed with ruddy colors from Nature's own palette, and carried the smile that knows no guile or pain, today burns consumingly in the torrid heat of the fever furnace. The little lips that yesterday pouted in happy contentment are now convulsively moved in painful grimaces. The eyes that before danced in innocent ecstacy today are pallid and heavy. Life in him finds little room and time for ornament and expression; it only seeks the right today to exist in the frail little vessel which Death would shatter and destroy.

To him comes the doctor, the old country doctor, that steady enemy of over-eager Death. And Death finds in this country doctor no mean antagonist. For though he fights single-handed, he fights with faith and open confidence, and his weapons are keened in experience and strong with steady use. Beside the bedside he sits now in pensive thought. He watches the patient from a background of a long and rich experience. Gently and painstakingly he proceeds to build his chain of tests and trials that will prove the nature of the grim disease. His stock in trade of laboratory adjuncts is the little glass instrument that records the fever's reaction, and the disc of taut celluloid that he presses over the heaving breast and connects with his own ears. He hearkens to the little heart's wild beat-

ings as it speeds in reckless pace to counteract the stifling toxins that would press its life away.

Through the pitter-patter of the rain drops upon the shingle roof he listens knowingly to the message of his deftly handled stethoscope. A measure then of the wrist pulsations, the ominous taps upon the heaving chest, a searching glance into the inflamed throat, the careful lifting of a heavy eyelid; these are the laboratory tests of this gentle man of science. Now and again a soft spoken question to the parents, and then some more percussion. Finally comes the diagnosis. No need has he of smeared slide or oil immersed lens, no loop or needle, blood or agar slant. His clinical laboratory is in and on his finger tips. Tension of alveolar air need find no record here by way of colorimeter or complicated tools. The child's dyspnea is "sign complete" to him of acid hunger. The apple-scented breath is proof enough of ketone crises. The fleeting heart, the creaky bronchioles, the rasping, unproductive cough, the damming of the lungs, proclaim to him in louder tones than all the tests of science. Pneumonia he calls it, and pneumonia it is.

Thus out of the maze of indifferent, confusing, misleading symptoms he unwittingly but unfailingly picks the presenting symptoms and goes on to the diagnosis. He cares not what numerical type the infection might be, nor what the "blood count" registers. Let the leukocytes carom in merriness and unnumbered as long as they attend to the business in hand. Let the mild-minnered guinea-pig and long-tailed mouse comfort and serve his more exacting brother practitioner in the scientific city, who wastes precious moments in confirming diagnoses when life may refuse to spare the time and wait.

In the cabin he is done for all time with the diagnosis. His is now the business of treatment. Carefully he opens the cabin windows in spite of beating rain. Out goes the humid mustiness of the heated indoors, and in comes the air of the highlands, clean with the fragrance of moist pines and spicy cedars. The old doctor now turns to his peripatetic dispensary and selects with evident care the weapons with which to fight the dread disease. Into a willow cup, half-full with crystal water, he measures the chosen tinctures. Then, when well mixed, he hands it to the mother, and with very definite instructions bids her to be regular in its administration. An admonition to keep the patient warm and quiet and free from draughts

terminates the visit. The doctor picks up his top hat and his precious medicine bag, and without ostentation hurries back to Dobbin and his other sick patients.

Not a word of hope or a promise to return has he left with the eager parents, but they know full well that he comes again tomorrow. In him amply rests their every hope. Well they know that if human skill can restore their only child to a measure of health again, his welfare rests in able hands. Their faith in the old doctor is sublime and beautiful. So they return to their vigil with fervent prayers on their lips and fulsome hope upon their breasts. And a listening, willing God sees to the fulfillment of their every hope.

That is the picture—in the backwoods of Kentucky, in the rolling plains of Michigan, among the pines of Pocono, along the shores of Maryland, out in the torrid sun of the prairies, in the broad wastes of the Texan sands, where the mesquite blows down Mexico way, between the snow-clad peaks of bleak Alaska—everywhere that men gather and rear their families—everywhere that sickness parades through human habitations.

The picture is no idle fantasy. But it is a picture that increasingly loses its reality. It is a picture that is soon to pass into oblivion.

For the leaders in medical training today have mapped for students of the profession an education that turns them out of the service of rural communities into the more specialized and easier task of attending to the bodily welfare of city dwellers. The road of the country doctor is too hard for them to travel, and there is little incentive for the highly trained graduate to seek his duties along the lonely trail that leads into gloomy hills.

The men presently responsible for medical training have scrapped without mercy the smaller schools that gave these countrymen their basic training. They have made it impossible for the smaller colleges to function, deliberately wrecked them—now the pendulum swings back again. The reaction from the insane superstandard pre-requisites is being felt. Men and women of the countryside have as much right to demand ready medical service as their brothers and sisters in town and city. And medical attention they will have.

Listen! Here is the message of the president of a large university delivered to a recent gathering of medical alumni: "We have

made the great mistake in medical education, we have set the standards uniformly high. We have throttled the lesser schools; we have failed to appreciate that we could not supply the demand for practicing doctors if we insisted on the rigid enforcement of our educational prescription. Let us go back to the lesser schools and give them the right again to train our doctors. We used to say that small schools did not turn out good doctors, but only half-trained doctors. But today we admit that half a doctor is better than not a doctor at all."

We take no issue with this gentleman's viewpoint, even if we do know that not all half-trained doctors have come from the smaller schools.

But we do feel that he has heard the call of the backwoods in Kentucky; he has sensed the cry of the sickly child and the beck of the waiting mother of the hillside cabin, and he knows that unless the bars are soon lowered there shall some day be no one to answer to the frenzied call.

He has seen the progress of the quack, the filling coffers of the charlatan—the isms, the cults, the paths and ics, and he knows their menace to honest medicine.

He has seen the writing on the wall, and he understands its meaning.

SOLID EXTRACTS

Cyclohexanol is made by reducing carbolic acid with nascent hydrogen. Perfumers find it useful as an essential oil solvent, and flower essences, no matter how delicate, seem not to be affected by it. This compound exerts a peculiar action upon soap, which with the addition of a small proportion of cyclohexanol becomes a solvent for hydrocarbon oils. Such soaps mix homogeneously with water and give a heavy lather.

Carrel-Dakin solution is not made by dissolving Chlorazene or Chloramine-T or any other organic chlorine compound in water. The pharmacist who advertently dispenses such solutions is not fulfilling his professional obligations, since these liquids are not in any way comparable, chemically or clinically, to the carefully prepared Carrel-Dakin solution of sodium hypochlorite.

The toxin which is secreted by the bacillus botulinus (a bacterial denizen of decayed foods such as sausage, fish, ripe olives, etc.) is stated to be the most powerful poison known.

Less than one drop of it is said to be sufficient to kill every human being on the face of the earth.

The blessed thistle (*Cnicus benedictus*) contains a peculiar enzyme similar to rennet, and which like rennet has the property of coagulating milk. Other common plants containing a similiar enzyme are jimson weed, the common fig tree, sundew and lupine.

Alcohol is the most promising understudy for gasoline as a motor fuel. The latter, if statistical data are to be relied upon, is due to wind up its career very shortly. Alcohol is very reluctant to ignite, but when ether or a similar compound is added to it, it becomes a little more tractable. Alcohol possesses many advantages over gasoline. For instance, it is not as inflammable, its flames may be extinguished with water and requires less air for complete combustion.

It is well to remember that quinine bisulphate under certain conditions of temperature is partly changed into quinotoxin, a very toxic substance. Ampules containing solutions of quinine bisulphate and acid quinine hydrochloride, sterilized in an autoclave, will often exhibit a yellowish color, due to the formation of this compound.

Can cows eat sawdust and thrive? Yes, if the sawdust is properly prepared! White pine sawdust when heated with dilute sulphuric acid and cooled with steam under pressure, undergoes a chemical change, being partially converted into glucose, a simple sugar which is digestible and nutritious. Neutralization with lime and concentration with heat affords a molasses-like substance, which is then mixed with the dried sawdust residue, producing a bran-like, palatable material.

Rest for the housewife weary from rubbing the family knives, forks and spoons is foreseen as a result of experiments at Sheffield, which indicate that the stainless metal, chromium, may be used in electro-plating. These experiments have crowned with success years of effort to find a method of depositing this valuable element on iron, steel, copper, nickel and brass by an electric current.

Chromium is harder and lasts longer than the rust-proofing metals usually used. As it resists oxidation by air, water and acids, chromium-plating may also be employed to make ordinary steel knife blades stainless, as well as for plating food tools and ornamental ware.

Prof. Ray Nelson, of Michigan Agricultural College, has discovered that protozoa, less than a hundred-thousandth of an inch thick, prey on plants and cause "calico-leaf" or "leaf-roll" just as the microbes, called trypanosomes, cause sleeping sickness in man.

Prof. Nelson, who, though only twenty-nine, has discovered that many illnesses of plants, similarly to those of people, are due to these microscopic animal parasites. He was the first to see and photograph these min-

ute organisms in potato, tomato, bean, clover and other plants affected by mosaic disease.

A compound has been produced from certain cells of the skate and tissues of some clams and found to reduce the symptoms of diabetes, the Department of Physiology of the University of Toronto has revealed.

Although the identity and composition of the substance is still unknown, it is similar in properties to insulin, which was prepared from the pancreas of animals and which has been found by experiments on men and animals to be a specific in the treatment of sugar diabetes.

A constituent of food, hitherto unrecognized, that animals must have before they can produce young, has been discovered by Dr. Herbert Evans and Dr. K. Scott Bishop, of the University of California. It occurs in lettuce and alfalfa, egg yolk and fresh meat, and as soon as Dr. Evans can establish its characteristics it will probably take its place in science as the fourth firmly established vitamin.

CORRESPONDENCE

Editor, THE AMERICAN JOURNAL OF PHARMACY.

Dear Sir:

On perusing the brief biography of John Chapman (Johnny Appleseed), appearing in the November issue of THE AMERICAN JOURNAL OF PHARMACY, there comes to my mind much of the verbal history of this strange character of the Middle West, who from about 1790 to 1830 did much for the frontiersmen along the Ohio River banks in the new country of the white man. Aside from distributing the seeds of apples and of many medicinal herbs, he also diffused through that countryside a great deal of religious knowledge. A very interesting phase of Johnny Appleseed's service is usually disregarded, but I believe that one can say, without fear of contradiction, that this quaint old gentleman was responsible for the organization of the first American circulating library, and he, himself, functioned as librarian-in-chief for more than three decades. Books in those days were very scarce, and to compensate for this scarcity Johnny would divide his books into their respective chapters and distribute these several chapters among the settlers, who, under his guidance, afterwards exchanged chapters one with the other, until the entire book had passed through the individual's hands. His favorite books were the Bible and the New Testament,

and in view of the numerous books of the Scriptures this peripatetic teacher had ample reading and exhorting material to submit to his circuit.

Visiting yearly or oftener, he kept the books circulating freely among the primitive settlers, who looked forward with great pleasure to his visitations. His method of teaching agriculturally, horticulturally and Scripturally was very emphatic. By one old settler, who apparently had some knowledge of anatomy, he was compared to the heart with its dual function, *vis a fronte,* drawing after him those who wished to follow, and *vis a tergo,* pushing along those who indicated a disposition to go slow or turn back. He was always welcomed as "bringing the latest news from heaven." He did not hesitate to visit other exhorters to gain new ideas and words and was frequently seen at the camp of Lorenzo Dowe, a Methodist preacher and a more educated man than Chapman.

It is said that on one occasion Lorenzo was explaining that the humble at heart should be modest in clothing to represent the primitive Christian, when Johnny Appleseed stepped out from a clump of bushes to where Lorenzo was standing on a stump of a tree speaking to his congregation. "Here," said Johnny, "is your primitive Christian," as he appeared on the stage dressed only in a coffee bag in which he had cut holes for head and arms. Little did Johnny suspect that he in his sparse clothing was blazing the trail for the ultra-fashionable debutante of the present day.

As I previously stated, the settler was always glad to have Johnny Appleseed as an over-night guest, and he, in return, was always glad of food and shelter. He showed them the art of planting crops and getting good returns, and often furnished them without cost with new seeds necessary for their pioneer ventures. When they deviated from his instructions in any way it is said that he chastised them kindly but emphatically. One can only look at these eccentric characters of early American days with much respect and esteem, and I am glad to know that Johnny Appleseed's grave is marked so properly by a glacial boulder, made smooth by much travel. For so also was Johnny Appleseed's character made smooth and worthy by constant service in the interests of his fellow men.

Yours very truly,

(Sgd.) C. C. Moore, M. D.

Philadelphia Pa.

SCIENTIFIC AND TECHNICAL ABSTRACTS

BREAKAGE OF WATCH-SPRINGS.—S. R. Williams, of Oberlin College, has investigated the cause of the spontaneous breaking of mainsprings in watches, a common and annoying incident. It appears that watch repairers are inclined to the view that such breakages are seasonal, occurring principally in the warmer months. Williams was permitted to examine the records over several years of two firms doing a large repair business, and on plotting the results found in both cases a peak in summer fairly coincident with the peak of the graph showing the occurrence of thunderstorms. There was, however, in both cases, a slight dip about mid-July, which has been ascribed to the absence of many persons on vacation. Herman Seemann, a pupil in advanced standing in the department of physics at the college, made experiments in the matter, and the results indicate that the breakage is not due to heat but to moisture. William thinks that the moisture acts by starting rusting points which weaken the spring at those points. In an experiment, in which fifty-six samples were tried, equally divided between two well sealed jars, one containing dry and the other moist air, seventeen springs broke in the latter and none in the former. Seemann also found that oiling the spring diminishes very markedly the liability to break.

H. L.

STUDIES OF SAPONINS.—At a meeting of the Austrian Pharmaceutic Society, November 8, 1922, Dr. Leo Kofler presented a communication on the saponins, under which title several similar substances existing in plants are included. They are characterized especially by the power of producing with water a durable foam and aiding the emulsification of oils. The solution is acrid, the powdered material excites sneezing, and has hemolytic action. Even very dilute solutions are poisonous to many fishes. Cholesterol counteracts this toxic effect. The chemical constitution is not clearly known. They are non-nitrogenous glucosides, yielding on hydrolysis a number of sugars. Structural formulas have been sug-

gested but not established, and even the empirical formulas are in some doubt as pure materials are not yet available. Most of the saponins are amorphous. (This is probably not an essential condition.) Several forms may be present in the same plant. The known forms may be classified as acid or neutral. The author of the paper described methods for the extraction of the substances. He advised the use of the hemolytic power as a means of detecting and determining them in plants. The foam-producing power may serve for detection of saponins in foods and beverages.—H. L. (The above abstract is from *Pharm. Monatsh.*, 1922, iii, 164.)

ANALYTIC FEES IN AUSTRIA.—The Austrian authorities have recently issued an official tariff of fees for some common analytic work which are rather startling at first sight. They are given in crowns (Kronen), the normal value of which is 20.3 cents, but which is now quoted in the American market at about 700 for a cent:

Deter. of alcohol by distillation	5000 K.
" " sugar without polarization	5000 K.
" " " with "	10000 K.
For a complete analysis of beer	15000 K.

At the quoted exchange rate, the fee for determination of alcohol would be about 7 cents. Examinations of price and fee lists in the countries having exceptionally low exchange rates show that in the domestic transactions a much higher relative value prevails than is indicated by rates on the American market. The above fees have no precise meaning unless compared with many other items of price, but they indicate in a general way the enormous inflation of the currency.

H. L.

PROGRESS IN NITROGEN FIXATION.—The annual report of the United States laboratory for research on nitrogen fixation, gives a summary of the work accomplished in the fiscal year ending June 30, 1922. The laboratory is under the direction of Dr. Cottrell, and is in the Department of Agriculture. The importance of the pro-

cedures for nitrogen fixation is pointed out. Three of these are at present prominent: direct union by the arc, production of cyanamide and synthesis of ammonia. Several others, Buchner (alkali-cyanide), Serpek (aluminum nitride) and Häuser (explosion) have been investigated and operated on fairly large scales, but cannot yet be considered commercially established. In the United States at present nitrogen compounds cannot be made by fixation at prices that will compete with Chile nitrate and ammonia from coal coking, except under unusually favorable circumstances. The special problem before the research worker in this field is to reduce the cost of the fixation methods. The synthetic ammonia (Haber) process is the one that presents especial advantages and difficulties. The principal difficulty is to secure a catalyst that may be easily obtained in quantity and that is not very sensitive to impurities. The laboratory has had considerable success in this line. The production of pure hydrogen and the discovery of a material for the containers have been also studied with encouraging results. Ordinary carbon steel soon deteriorates under the conditions in which the gases are combined. The development of apparatus capable of bearing a much higher pressure has been undertaken, inasmuch as combination is greatly favored by increasing pressure. Studies of the cyanamide method have not so far indicated any considerable reduction of cost. The arc method has the advantages that it can be installed rapidly and delivers the nitrogen directly in the oxidized condition. The direct cyanide (Buchner) method has not been successfully developed on a commercial scale. The chemical and engineering features require further study. There is some doubt whether the product of the cyanide process can be converted cheaply into fertilizing material, but it must be borne in mind that the recent application of hydrogen cyanide as a fumigating agent for fruit trees has developed a new and rapidly growing market.

Comparatively little information is at hand as to the agricultural value of many of the compounds obtained by nitrogen fixation, for which reason an experimental farm has been installed. Interesting and valuable results have already been obtained and are being prepared for publication.

H. L.

MEDICAL AND PHARMACEUTICAL NOTES

RECENT INVESTIGATIONS OF ANTHELMINTICS.—An abstract of a report from the Wellcome Chemical Research Laboratories, published in *J. S. C. I.*, 1922, v. 41, 467a, gives interesting information concerning the treatment of the more important parasites inhabiting the human intestine. Of these, the several species of hook-worm are probably of most frequent occurrence, and constitute the most serious form. The data of the report are from the observations of Dr. F. A. Miller in Colombia, this work being one of the many campaigns under the auspices of the Rockefeller Foundation. Out of over 53,000 persons examined, 93 per cent. were infected. Nearly all of the infected ones were treated and 78 per cent. cured. The number of people now being treated in the different parts of the world in which the infection occurs is probably several millions, and these represent but a small proportion of those needing treatment. Everyone engaged in the work recognizes the necessity of prevention, but sanitary rules stringent enough to prevent infection are very difficult to enforce among the people who need them. Two distinct species of worm are encountered: *Ancylostomum duodenale* and *Necator americanus.*

The drugs used must be quite safe. Many have been recommended, but in the treatment of hookworm beta-naphthol, thymol and chenopodium oil have been extensively used. Chenopodium oil was examined recently in the Wellcome laboratory, its constituents isolated and tried in Brazil by Dr. Smilie. The clinical results are not yet published but it has been found that the sole constituent of the oil efficient against hookworm is an organic peroxide, ascaridole, which is present in different amounts in different samples, a fact that accounts for the irregular results often obtained. Ascaridole is somewhat unstable and is liable to be decomposed into inert substances on distilling. Hookworm infection is in the main a tropical disease, though not wholly unknown in temperate regions. Carbon tetrachloride is the latest remedy and good results have been obtained with it.—H. L.

STUDIES OF VITAMINS.—At a recent meeting of the Royal Institution of Great Britain, Dr. Arthur Harden presented a summary of present knowledge on the question of vitamins. Experiments on these substances are difficult and tedious. It seems to be established that vitamins A and C are fairly resistant to moderate increase of temperature provided air is excluded, but deteriorate rapidly when exposed to oxidation. Vitamin B is less affected by heat and aeration. All three vitamins originate in the vegetable kingdom, and in view of this fact, it is interesting to recall the Biblical endorsement of the "green herb for meat" as given to the residents of Gan-Eden. In fats, the vitamin seems to reside entirely in the unsaponifiable portion, and as this usually consists largely of cholesterol, which has no value, it is evident that the amount of the really active substance is very minute. Vitamin A does not appear until the photosynthetic actions occur. Vitamin C is not in seeds, but appears when they germinate and before any green parts are formed. The conditions under which vitamin B is produced are still somewhat uncertain, but its existence in yeast shows that it may be produced without action of light. Milk from stall-fed animals is poor in A and also likely to be deficient in C. The comparatively enormous amount of A in cod liver oil has been one of the most striking results of recent investigations, but in connection with these data the fact that liberal exposure to sunlight will often counteract certain dietetic deficiencies must not be overlooked. It must not be forgotten that most of these feeding experiments are conducted in laboratories not open freely to sunshine and that the animals are under decidedly unnatural conditions in some ways.—H. L.

DISTRIBUTION OF AMYGDALIN, PRULAURASIN AND SYNAPTASE IN BITTER ALMONDS AND CHERRY-LAUREL LEAVES.—Rosenthaler and Seiler (*Ber. d. Deut. Pharm. Gesell.*, 1922, xxxvii, 245 *et seq.*) report studies on this question. They used as a test the fact that when starch grains, faintly colored by iodin, are brought in contact with even a minute amount of hydrogen cyanide the color is discharged. The investigation was made by examining sections of the several parts of the plant mixed with a suspension of iodized starch grains.

To this mixture placed on a slide a drop of a 1 per cent. solution of synaptase in a 50 per cent. glycerol-water mixture was added, the cover glass laid on and again removed and applied, by which an intermixture can be easily obtained. This prevents error from the movement of the liquid. It is important that a large number of starch grains should be used, in order that the liberated cyanide should surely encounter them. The glycerol prevents too rapid diffusion. The iodized starch does not interfere with the action of the enzym. The bleaching is easily noted, especially as it is preceded by intermediate violet tint. The reaction is very delicate, as cyanide can be detected in pear seeds, which give only mere traces of it. The degree and rate of discoloration are dependent on the amount of cyanide produced, and, therefore, a measure of the amount of glucoside present. One disadvantage of the test is that some other substances discolor iodized starch, but this fallacy does not affect the research in question, as such substances have not been found in the tissues examined.

The results of the tests were: Amygdalin is present in most parts of the bitter almond, except the shell, and the percentage is not uniform in any given tissue but varies from cell to cell. Examinations of cherry-laurel leaves were made in March and showed that the glucoside (prulaurasin) was not present in the upper and lower epidermis, except in a few special cells. The chlorophyl parenchyma contains the glucoside, but the cells holding oxalates do not.

The distribution of the enzym, synaptase (emulsin) was also studied. It was found in all the parts of the bitter almond except the shell. In cherry-laurel leaves it was found in the same tissues as contain the glucoside. It might indeed be expected that the glucoside and its catalyst would be found associated.

INSULIN: A DIABETIC REMEDY.—Diabetes is one of the more serious afflictions of mankind, insidious in its beginnings, debilitating in its course, and often fatal. At present the treatment is little more than an effort to prolong life by a regimen of habit and diet so arduous as to make it very irksome. Dr. F. B. Banting, a young physician attached to the University of

Toronto, acting on the known fact that extirpation of the pancreas in dogs is followed by a diabetic condition, thought it possible that the secretion discharged into the blood by that gland might be the factor inhibiting the onset of the disease, and that its administration in some form might prove a remedy. Experimental work confirmed his theory, which has, in fact, been thought probable for many years. A substance, to which the name "insulin" has been given, extracted from the pancreas of the ox, pig or sheep, when injected into the veins of human diabetic patients, has frequently given quick relief, and has appeared to lead towards cure. But the remedy is still in an early stage. The exact constitution of insulin, as, indeed, of many other of the subtler animal essences, is still unknown; its preparation demands high skill and special methods; its administration must be watched by expert physicians. In the opinion of the medical faculty of the University of Toronto, of their American colleagues and of representatives of our own Medical Research Council, any premature exploitation of insulin might gravely disappoint the public, and even prevent the ripening of the hopes of these high authorities. It has therefore been decided to protect and control its manufacture and use in the United States and in Canada. Similar protection and control in this country have been offered to and accepted by the Medical Research Council. To protect the public and to perfect a great boon are objects which command respect. But while recognizing that special circumstances may in this case justify it, we are not entirely reassured about the method—a feeling that seems to have given an apologetic tone to the communication issued by the Medical Research Council. For it is proposed to patent the remedy—a course excluded from the practice of the Pasteur Institute. Pasteur and Metchnikov determined that their discoveries should be offered as a free gift to the world, although the possibilities of fraudulent or foolish exploitation by others, of mistaken use, and even of employing the revenue from patents for further research were present to their minds.—*The London Times.*

SPECIAL LABORATORY PROVIDED FOR THE COMMISSION ON CODEX.—Great satisfaction is expressed by French pharmacists on account of the happy and much needed innovation of an official

laboratory for the use of the Commission on Codex, the lack of which has long been deplored.

In consequence of this excellent step the director of the laboratory in question becomes a member of the Commission, and will be enabled to harmonize and unify the work eliminating errors and defective methods.—(*Répertoire de pharmacie.*) W. H. G.

On the Parasitic Action of Penicillium Glaucum and Mucor Stolonifer.—These two mushrooms are parasitically active with certain fruits, ripe or green (pears, apples, tomatoes), producing more or less active decay. The expressed juice of these decayed fruits is capable of attacking finely chopped healthy tissue, and disorganizing it. This is probably due to certain diastasis secreted by the mushrooms in question.—(M. Nobecourt in *Journal de pharmacie et de chemie.*) W. H. G.

Quinosol is the Neutral Sulphate of Orthooxyquinolin.—Used as a preservative, it produces very little modification with serums, and particularly with specific serums, leaving intact certain antibodies, notably the haemolytic antibodies. Quinol possesses anti-putrescent and inhibitive properties to a remarkable extent when used in very small quantities.—(*Journal de pharmacie et de chemie.*) W. H. G.

BOOK REVIEWS

Food Products from Afar. By E. H. S. Bailey, Ph. D., Professor of Chemistry, University of Kansas, and Herbert S. Bailey, A. B., B. S., Chief Chemist of The Southern Cotton Oil Company. Octavo, over 50 illustrations from photographs. 287 pp. Cloth, $3.00. The Century Company, N. Y. City, 1922.

The aborigine set up his tent where the mountain brook splashed into the lake or near the trail of the forest deer, the easier to obtain

his daily food. The early settlements were located at fords or at the junction of beaten paths where folk stopped to buy and sell produce. Cities sprang up at the country crossroads, because there the farmer met the merchant that they might barter with one another. Today our nation stands at the intersection of the world's trade-routes and we may take toll of all the earth's foodstores.

A knowledge of "what other people eat," just as of what they think and say, is of practical interest. We may also learn something of the composition and dietetic value of these foreign foods, so as to select them judiciously and use them economically. Spices from India, macaroni from Naples, rice from Japan, oils from Italy and Spain, tea from China, cheese from France, coffee and bananas from Latin-America—little do we realize how much we owe of the variety and flavor and quantity of our foods to other lands. In this thoroughly accurate and altogether popular book two food experts, both chemists of high standing, present the subject of "Food Products From Afar."

The book also abounds in historical data, as, for instance: Story of the Discovery of Macaroni, Use of Oils by the Ancients, Legends of the Date Palm, History of the Early Use of Rice, Origin of the Sugar Cane, History of the Pineapple, History of the Use of Coffee and Tea, etc.

We can highly recommend this book to pharmacists.

OTTO RAUBENHEIMER, Ph. M.

LUTFADEN DER KOSMETIK FUR AERZTE, von Prof. Dr. Fritz Juliusberg, Braunschweig. Octavo, 144 pp., 12 illustrations. Urban & Schwarzenberg, Berlin and Wien, 1922.

The art of beautifying mankind, or rather womankind, as old as it is full of error, as keenly sought after by young and old as it is practiced by avaricious men of the commercial world, has long been identified with the mystery of how to renew one's youth. It seeks refuge among the various costly bottles and powder-boxes which adorn the elaborate toilet tables of the gentler sex. But as in all departments of modern social life, so also here has science penetrated into the very heart of things. No longer has cosmetics for

its aim and object such follies as the renewal of youth, but it has become a definite branch of medical research, and has shown that the preservation of beauty is an obligation and a sacred duty which we owe to our bodies.

Not only the physician but also the pharmacist should be acquainted with the subject of cosmetics, and the little book before us is an estimable text for this purpose. It contains numerous prescriptions and many difficult ones, with which the pharmacist should become acquainted. One page of the book is devoted to the literature on cosmetics, a very valuable addition.

OTTO RAUBENHEIMER, Ph. M.

THE HISTORY OF MEDICINE IN ITS SALIENT FEATURES. By Walter Libby, M. A., Ph. D., Univ. Pittsburgh. Octavo, 427 pp., illustrated. Cloth, 3.00. Houghton Mifflin Co., Boston and New York.

The volume before us is the result of the lectures on the history of medicine, delivered by the author since 1918. The subject is treated very completely, as can be seen from the following twenty chapter headings: Priest-Physicians of Egypt and Babylonia; Hippocrates, the Father of Medicine; Roma Anatomy and Surgery; The Transmission of Medical Science by the Arabs; Revival of Anatomy and Surgery in the 16th Century; William Harvey and the Revival of Physiology; Science and Practice: Sydenheim and Boerhaave; Comparative Anatomy: John Hunter; Morbid Anatomy and Histology: Morgagni and Bichat; Local Diagnosis: Auenbrugger and Laennec; Advances in Physiology, Embryology, and Karl Ernst von Baer; The Cell-Theory and Cellular Pathology; Introduction of Anæsthetics; Theory of Organic Evolution; The Founders of Bacteriology; Antiseptic Surgery: Lord Lister; The History of Syphilis; Preventive Medicine in the Tropics, and Medical Science and Modern Warfare.

A decided advantage of the book is the list of references given at the end of each chapter, thus enabling the student and reader to peruse the subject still further. With his luminous exposition of

the growth of medicine, the author interweaves a generous amount of biographical data concerning the great men who have made this growth possible.

Medicine and pharmacy go hand in hand. The history of one is the history of the other profession. For that reason Libby's History of Medicine is a book well suited for pharmacists.

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